

Journal of The Franklin Institute

Devoted to Science and the Mechanic Arts

Vol. 192

JULY, 1921

No. 1

CHEMICAL FACTORS IN NUTRITION.*

BY

LAFAYETTE B. MENDEL, Ph.D., Sc.D.

Professor of Physiological Chemistry, Yale University, New Haven, Conn.

WHEN the food which we ingest starts on its way along the path of the alimentary tract it is ordinarily regarded as having entered the body. It does, in truth, disappear from sight as soon as it has passed beyond the mouth and into the deeper recesses of the organism; but every one who is familiar with the structure of the long gastro-intestinal tube—the digestive canal—realizes that the walls of the latter offer a pronounced barrier to the ready transport of the swallowed food materials to the various tissues and organs where it may be needed. To follow the nutrients into the stomach and upper intestine is comparatively easy; far more difficult, however, is the task of tracing their passage through the thick walls of the alimentary tract into the lymph and blood-streams wherein they are distributed far and wide in the body.

Insoluble food particles obviously cannot permeate the mucous membrane that lines the enteric tract. The older physiologists, who concerned themselves not at all with the problem of how such solid nutriment is made available, were content to assume that in some way it must become soluble so that it can filter or diffuse through the gastro-intestinal wall. Some sort of digestion was thus conceived to be essential to absorption in the case of insoluble products such as much of an ordinary meal represents. For a long time it was vigorously debated whether digestion in the

* Presented at a meeting of the Section of Physics and Chemistry held Thursday, March 10, 1921.

[NOTE.—The Franklin Institute is not responsible for the statements and opinions advanced by contributors to the JOURNAL.]

COPYRIGHT, 1921, by THE FRANKLIN INSTITUTE.

VOL. 192, No. 1147—I

25654

stomach, and perhaps beyond, was not secured by mechanical trituration of the food or by some fermentative processes. It redounds to the credit of the progress of science in America that this country early furnished one of the great classics in the study of physiology of digestion. The pioneer investigations of Dr. William Beaumont on Alexis St. Martin, the man with "the lid on his stomach," helped to elucidate the nature of the gastric juice and establish the fact that it is an "agent of chymification" which "acts as a solvent of food and alters its properties." Experiment thus replaced conjecture.

The familiar foodstuffs—the proteins, fats and carbohydrates—which in large measure compose our food, are not simple chemical substances; they are for the most part rather complex compounds. With the development of the physiological chemistry of digestion has come the growing recognition that all the foodstuffs not merely are dissolved, but are further chemically disintegrated before they experience absorption. This profound cleavage of the nutrients into relatively simple fragments is accomplished by the unique potency of the digestive juices. In my own student days it sufficed to believe that the digestion of proteins, accomplished by the proteolytic enzymes or ferments of the gastric and pancreatic secretions, transformed the albuminous substances into proteoses and peptones, still essentially protein in nature except for a greater diffusibility, and perhaps to a smaller extent into a few then recognized amino-acids. Foster's "Text-book of Physiology," a popular treatise of a quarter of a century ago, stated:

In all events the greater part of the proteid material of the food enters the blood as proteid material either as peptone or in some other form, and is carried as proteid material to the tissues. * * * The evidence as far as it goes tends to show that the metabolism of proteid is very complex and varied, that a large number of nitrogen-holding substances make a momentary appearance in the body, taking origin at this or that step in the downward steps of katabolic metabolism and changing into something else at the next step, and that the presence in various parts of the body and even in the urine, in small quantities, of so many varied nitrogenous crystalline substances, forming a large part of what are known as extractives, has to do with this varied metabolism. Possibly the transformations by which nitrogen thus passes downward take place to a certain extent in such organs as the liver and the spleen, which are remarkably rich in these extractives. But the whole story of proteid metabolism consists at present mostly of guesses and of gaps.

To-day there is added the knowledge of the further peculiar proteolytic power of the intestinal secretion, with the possibility

of a more or less complete disintegration of proteins into their constituent amino-acids prior to absorption. So, too, the fats are digested, not merely dissolved or absorbed in particulate form; and the carbohydrates pass through the alimentary wall as simple monosaccharide compounds. The true nutrient units discoverable after absorption in the blood-stream are comparatively simple chemical compounds rather than the complex food substances which we ordinarily ingest. Hence there is a significant truth in the recent statement that "the tissue cells never know the food which we eat." Digestion, profound in its chemical cleavages, is recognized as the indispensable forerunner of absorption.

The outcome of the digestive disintegration of the ingested foodstuffs is, therefore, somewhat different from what one would have assumed only a few years ago. The ultimate sources of energy for the organism start as relatively simple chemical compounds on the path of distribution to the places where they are required for fuel or constructive enterprises. Amino-acids, other nitrogenous units like purins or nucleosides, simple sugars, and fats represent the particular types of matter that enter the transportation routes of the circulation. Sometimes they are built selectively into desired structures—into tissue fabrics or components of secretion; sometimes they are stored in special depots as fat or glycogen or protein to await a future demand for these reserves; sometimes they are at once consumed or, to quote the term used by the physiologist, they are metabolized.

The various aspects of life, like other activities in the world about us, represent a transformation of matter and energy. Our organism builds up and in turn wears out its structural parts, it utilizes food fuel somewhat as non-living mechanisms employ coal, wood, oil or gas. From this general standpoint the preceding review of the preparation of our food for distribution and subsequent use is not difficult to appreciate. It is only when the subtle details are contemplated that the innumerable intricate problems of nutrition present themselves. How does the organism build the absorbed nutrient units into suitable anatomical structures, or how does it transform them so that work is done and heat produced? The analogies of the steam engine with its fire box and fuel and air supply leave us in the lurch when we attempt to institute a strict comparison with the living organism. Indeed it may as well be admitted that the complete history of the physio-

logical metabolism of matter is still obscure and unrevealed. From time to time, however, new details have come to light, revealing some of the secrets of the chemical processes upon which life depends. Let us turn our attention to a few of these.

There are organisms which can satisfy their biological needs with a comparatively few substances of relatively simple character. Thus the yeast plant can be made to grow and complete its life cycle in a medium that furnishes only comparatively simple compounds—a little pure sugar, nitrogen in the form of ammonium sulphate, along with phosphates and chlorides of potassium, calcium, and magnesium. Development under these circumstances means profound chemical synthesis. The yeast organism builds up highly complex proteins, fats, carbohydrates, nucleic acid and presumably a multitude of as yet unrecognized compounds into the tiny cells that seem so simple and relatively undifferentiated to an observer through the microscope. Plants in general possess such remarkable powers of synthesis—mysterious and never failing in their wonders. The carbon dioxid of the air suffices to furnish carbon for most elaborate structures. Such well-recognized atmospheric sources of plant nutriment were scarcely dreamed of by the older investigators who searched for a “principle” of vegetation to account for the phenomena of soil fertility and plant growth. Van Helmont considered he had found it in water, and thus records his famous Brussels experiment :

I took an earthen vessel in which I put 200 pounds of soil dried in an oven; then I moistened with rain water and pressed hard into it a shoot of willow weighing 5 pounds. After exactly five years the tree that had grown up weighed 169 pounds and about 3 ounces. But the vessel had never received anything but rain water or distilled water to moisten the soil when this was necessary, and it remained full of soil which was still tightly packed, and, lest any dust from outside should get into the soil, it was covered with a sheet of iron coated with tin, but perforated with many holes. I did not take the weight of the leaves that fell in the autumn. In the end I dried the soil once more and got the same 200 pounds that I started with, less about two ounces. Therefore the 164 pounds of wood, bark, and root arose from the water alone.

The animal organisms, on the other hand, are not endowed with capacities for constructive work equal to those possessed by plants. It is not merely nitrogen, carbon and oxygen in some simple groupings that they require to be elaborated by them synthetically into brain and muscle and gland components. The powers of synthesis in animals are limited. Bathed though they

continually are in a sea of nitrogen, they cannot utilize it to produce nitrogenous tissues. There are certain structural units which the animal cannot manufacture *de novo*. Unless these are supplied as such, growth, tissue construction and repair are limited to the available supply of the essential parts.

The evidence for this conclusion forms a comparatively recent chapter in the study of nutrition. The nitrogenous needs of an animal can be supplied by the inclusion of protein in the diet. The newer chemistry of the proteins has brought unexpected revelations regarding their intimate structure and has thereby completely altered the traditional views regarding their physiological behavior. It has been demonstrated that, in general, the proteins are complexes which yield eighteen or more amino-acids that have become prominent items of interest to the student of nutrition. The proteins from different sources, and likewise the different proteins from a single plant or animal tissue, may vary in respect to the proportions of the characteristic amino-acids—the constructive units or “building stones” out of which they are built up. Some fail to yield one or more of the amino-acids usually obtainable from proteins. In this sense they are sometimes spoken of as “incomplete” proteins. For example, of the usually obtained representatives, the protein zein of the maize kernel fails to yield either glycocoll, lysine, or tryptophane; the gliadin of wheat is comparatively poor in its contribution of lysine and extremely rich in the glutaminic acid group; the gelatin derived from connective tissue lacks the tyrosine, tryptophane and sulphur-containing cystine groups.

With the possibility of such inequalities in the protein intake presented to the organism, how are we to conceive of the production or maintenance of blood- or muscle- or nerve-protein having the unvarying and specific chemical character that biological experience leads us to expect? For the answer to this question the modern chemistry of digestion has given a clue scarcely anticipated a generation ago. It has demonstrated that the various proteins are disintegrated in the digestive processes into their constituent amino-acid groups. It is, for the most part at least, these amino-acids rather than proteins *per se* that are absorbed and represent the ultimate alimentary contribution from the ingested proteins. The amino-acids are the fragmentary units in the form of which the albuminous intake is distributed throughout the body. From such fragments every individual tissue can select the con-

structive "building stones" which are specifically needed. Protein metabolism has thus become essentially a question of the behavior of amino-acids in the body. As I have expressed it elsewhere:

To-day we are concerned with the question whether this or that protein, whatever its biologic origin, will yield the characteristic desired, amino-acids, such as tyrosin and tryptophan, leucin and lysin, glycoll and cystin, histidin and arginin. Our attention is fixed on the building-stones or units out of which the great protein structures are put together. Instead of referring to the proteins in terms of their physical properties or empirical composition—their content of carbon, hydrogen, oxygen, nitrogen or sulphur—at least so far as the problems of nutrition are involved, the time has arrived for estimating their behavior in the organism on the basis of the quota of each of about eighteen well-defined amino-acids which the individual representatives of this group of foodstuffs can yield. Most, if not all, of these amino-acids are essential for the construction of tissue and the regeneration of cellular losses. In proportion as any specific protein can furnish these constructive units it may satisfy the nutritive needs of the body. The efficiency of the individual protein in this respect must depend on the minimum of any indispensable amino-acid that it will yield; for it is now known that some of them cannot be synthesized anew by the animal organism. If, for example, a protein or mixture of proteins comparatively deficient in their yield of the sulphur-containing amino-acid cystin be furnished alone to supply the body's nitrogenous requirements, the production of new, cystin-yielding molecules of protein will be limited by the amount which is available in the diet. An excess need not be wasted, for it can be burned up like sugar or fat to provide energy; but new construction or growth is limited by the minimum of the essential unit.

The views just amplified have been substantiated by the more recent investigations in nutrition, particularly in the feeding of laboratory animals such as rats and mice. Thus, with an otherwise adequate diet the nitrogenous factors can be suitably supplied by proteins isolated from a considerable diversity of both animal and plant sources. The list includes such representatives as casein (milk), lactalbumin (milk), ovalbumin (hen's egg), ovovitellin (hen's egg), edestin (hemp-seed), globulin (squash-seed), excelsin (Brazil-nut), glutelin (maize), globulin (cotton-seed), glutenin (wheat), glycinin (soy-bean), cannabin (hemp-seed), as well as the total proteins present in various animal and plant tissues such as meat (muscle tissue), liver, kidney, brain, peanut, soy-bean, cotton-seed, etc. In contrast with the growth of white rats, for example, to adult size on mixtures of isolated food substances containing any one of the above as the chief source of protein in the diet is the failure to grow on foods containing other proteins which have a recognized deficiency in their amino-acid make-up, *i.e.*, "incomplete" proteins.

In every-day life neither man nor animals ordinarily eat a single type of protein or even proteins from a single source. The intake consists, rather, of a mixture of proteins rarely, if ever, including only such as are entirely deficient in their amino-acid make-up from the physiological standpoint just defined. Nevertheless there may be a *relative* deficiency of some essential nutrient unit or "building stone" in comparison with the amount of other essentials. Building progress—tissue construction—may then be retarded by the lack of proportionate quantities of all the needed parts that cannot be synthesized directly by the body.

An apparent exception to the demonstrated need of supplying all nitrogenous essentials more or less ready-made to the animal organism has been recorded in certain ruminants. Sheep have been observed to gain many pounds over considerable periods of time on a diet of starch, denitrogenized straw, inorganic salts and urea, an exceedingly simple nitrogenous compound that readily disintegrates to form ammonia and carbon dioxide. A consideration of the peculiar anatomical arrangement of the alimentary tract of these animals serves to explain the possibility of such an outcome. In the first stomach of the ruminants, the rumen or paunch, opportunity is afforded for micro-organisms to thrive in the warm reservoir where the food mixtures are temporarily incubated, so to speak. Bacteria can and do grow luxuriantly there. Subsequently when the products of microbial activity including an enormous increment of bacterial bodies are moved along to the true, acid-secreting stomach, the bacteria, rich in newly synthesized protein-containing protoplasm, die and liberate the bacterial protein for use by the organism of the host. This is a unique instance of apparent protein synthesis by a higher animal, explicable however on the basis of the symbiotic action of bacteria. The same result could not be expected in man, because his food passes directly into a chamber, the stomach, provided with bactericidal facilities in the acid gastric juice.

Even when the dietary food proteins are selected with a view to furnishing an adequate supply of all amino-acids known to be requisite, the nutritive processes of the body may exhibit defects not of supply but of utilization. A fire box may be equipped with a certain type of grate to burn coal of various sizes. If the grate is changed smaller sizes of fuel like pea coal may escape combustion by falling into the ashpit. So it happens that under as yet obscure conditions certain amino-acids fail to be completely

consumed or utilized in the metabolism. Consequently they are eliminated more or less unchanged with the waste products. Cystinuria and alkaptonuria represent illustrative instances.

There are other cases in which a presumably adequate intake fails to unfold its entire nutritive possibilities because some defect in the organism interferes with complete conversion of some ingredient. There are times when fats may fail of digestion and absorption. They then make their way through the entire length of the digestive tract, finding a way out with the stools. The disturbance or difficulty is one of digestion or alimentation. However, the fats may be digested, absorbed, and transported only to meet with inadequate chemical destruction in the usual reactions that liberate energy. Products of incomplete combustion arise, just as they do in the coal fire or gas engine. There may arise acetone, diacetic acid or betaoxybutyric acid, substances that are physiologically offensive and objectionable, that may induce an "acidosis," and that are speedily eliminated as well as possible.

Again, who is not familiar with the common condition known as diabetes in which sugar is not properly metabolized or stored in the body? There are in this country alone more than half a million diabetics, persons who fail to burn up one of the most common of food fuels. Striking statistics gathered by Doctor Joslin, of Boston, a conscientious student of diabetes, show an undeniable association of obesity and diabetes. It appears that persons above the age of fifty rarely acquire the disease, *i.e.*, the inability to burn certain kinds of food fuel well, if their weight is not above normal. Joslin writes:

Diabetes is largely a penalty of obesity, and the greater the obesity, the more likely is Nature to enforce it. The sooner this is realized by physicians and the laity, the sooner will the advancing frequency of diabetes be checked. The penalty of taking too much alcohol is well known, and a drunkard is looked on with pity or contempt. Rarely persons who become fat deserve pity because of a real tendency to put on weight despite moderate eating, but usually most should be placed in somewhat the same category as the alcoholic. In the next generation one may be almost ashamed to have diabetes. It is all nonsense to use polite terms for being "just fat." It is generally prudent and always far more effective to say to the patient: "You are too fat," than cautiously to remark: "You are a trifle obese." Fat diathesis! Granted there is one person in a thousand who has some inherent peculiarity of the metabolism which has led to obesity, there are 999 for whom being fat implies too much food or too little exercise, or both combined.

Successful nutrition therefore not only demands the nutrient units properly digested and absorbed but also entails an organism in functioning condition to dispose of them. A water-power plant may become impaired not only when the supply reservoir runs low but also when its turbines or energy-converters are defective. But proteins and fats and sugars and their immediate chemical relatives are not the only indispensable factors in a successful diet. Present day physiology—again largely a product of the work of American investigators—has demonstrated the dominant importance of certain inorganic factors—of calcium phosphorus, chlorin, etc., and has given striking evidence of the rôle played by the so-called vitamins. The spark plug and lubricants help to make effective the energy stored in the gasoline supply of a heat engine. In nutrition likewise there are “accessories” without which the animal mechanism fails to run smoothly. The story of their importance may already be found portrayed with almost dramatic effect in the popular literature of the day.

It is instructive to follow the reaction of the public and the professions dealing with nutrition to each progressive step in the understanding of the nutritive functions. When the extent to which digestion occurs in the alimentary tract began to be disclosed by adequate experiments the predigestion of foods was promptly advocated, particularly for the sick and the young supposedly equipped with only feeble digestive apparatus. Meat and wheat and milk were prepared in a diversity of predigested forms by the physician, by the layman acting on his advice, and by the manufacturer.

To-day few remember the multiplicity of unpalatable products that were advertised and advocated a generation ago. In those days one might have spoken of foods “predigested to absorb” as nowadays one is reminded of foods “cooked ready to serve.” No one seems to have asked whether the human alimentary tract was often so enfeebled as to require digestive help, or whether the exercise of the digestive function were not beneficial rather than baneful. Disuse of some organs leads to atrophy. An unexercised muscle becomes flabby. With the waning prominence of predigested foods, “isolated” foods, and notably protein food products waxed in popularity. The protein of pot cheese was sold at liberal profits, as a dietary supplement, mostly to the highly educated classes who are sometimes also highly credulous. At

present we are threatened with an avalanche of vitamine preparations. Somehow the drug store always manages to compete with the butcher shop and grocery, even in the domain of dietetics.

Students of nutrition are sometimes asked how it happens that nations have been so successfully nourished in the past despite the lack of knowledge of what are now regarded as fundamentals of nutrition. A partial answer has been formulated by Professor Hopkins:

In many departments of human knowledge the teaching and guidance of science are accepted as final because in these departments the knowledge arose in the first instance from scientific studies and from these alone. Progress in such categories depends entirely upon controlled and recorded observation or upon experiment, and these are the methods of science. It is otherwise, one might be tempted to say, in regions where mankind can claim abundant and accumulated empirical experience. In connection with his own nutrition man's experience has been—needless to say—coterminous with his whole existence. Science may explain that experience, but is unlikely, it might seem, to improve upon experience as a guide. It may supply theory, but where experience has been so great and so continuous it seems unlikely that it could do much to guide practice. This consideration, consciously or subconsciously, accounts, I think, for a widespread feeling that the teachings of science about our food supply are of academic interest only.

We may hasten to add, however, that when peoples are forced to depart from the traditional practices that experience has shown to be safe, danger may arise. This is what happened in such unfortunate ways during the war. It is what may happen anywhere whenever persons depart from established and well tested customs to enter novel paths. Thus the substitution of polished rice for the unmilled variety led to nutritive disaster, often told in the story of beriberi. Pellagra has a related history. Rickets has a background of defective diet. Scurvy, too, attends the neglect of conventional modes of feeding. There is, then, room for a science of nutrition even in the domain of practical dietetics. Not all nations bungled their food problems during the war. How our British allies feel has lately been expressed by Professor Halliburton:

Lord Rosebery, in a sentence that has stuck in our memories, said some years ago that "we generally muddle through somehow," but in connection with food there has been in this country a minimum of muddle, rationing has gone smoothly, there has been but little hardship, and we are through. How far physiology has been instrumental in helping to bring about this happy result I may safely leave to the judgment of others.