A History of Nutrition Research Reflected in the USDA Tables of Food Composition

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Nutrient Analysis

Aristotle (384-322 B.C.)(Fig. 1) was the first to suggest that the composition of foods in the normal diet might contribute to health. He believed that the forms and sources of nature included the contrary principles of "dry" and "moist" and "hot" and "cold." Out of this concept of opposites Aristotle defined the four principles, fire, air, water, and earth, which he believed were the basic components of the body (Fig. 2). This theory of body composition was accepted for more than 2,000 years and still exists as a folk belief in many of the world's cultures. A physician, Empedocles, subsequently borrowed this theory, transforming the four elements into the four humors: yellow bile (hot, dry), blood (hot, wet), black bile (cold, dry) and phlegm (cold, wet). The combination of the humors determined a person's health and temperament.(1)

Hippocrates (Fig. 3), born in 460 B.C., hypothesized the existence of a connection between diet and health, and although skeptical about the theory of the humors, suggested that diet was linked to them. He wrote that "growing bodies have the most innate heat; they therefore require the most food for otherwise their bodies are wasted. In old people the heat is feeble and they require little fuel, as it were, to the flame, for it would be extinguished by much." Further, "persons who are naturally very fat are apt to die earlier than those who are slender."(2)

Phase I: Macronutrients

Antoine Laurent Lavoisier (1743-1794) (Fig. 4), the founder of the sciences of chemistry and nutrition,(2) was the first to use chemical methods to demonstrate the quantitative relationship between carbon oxidation and heat production in fire. Further, he demonstrated this relationship in the combustion of carbon in animals and measured CO_2 production in man. Jean Baptiste Boussingault (1802-1887) (Fig. 5) employed the methods of organic chemical analysis developed by Lavoisier and his students to conduct the first "balance" studies of an animal's intake and excretion of elements as measured in food and excreta. In 1839 he determined the quantity of carbon in a cow's fodder and in its urine, feces, and milk.

It has been said that chemistry is a French science, and the French certainly led the way during the era of Lavoisier and his students Boussingault and Gay-Lussac. But the chemistry mantle passed to Germany with Gay-Lussac's pupil, Justus von Liebig (1803-1873) (Fig. 6). Liebig perfected Lavoisier's methods for analyzing organic substances, and he was the first to apply the balance method to investigations in humans. In fact, he determined the carbon balance of an entire company of the Ducal Guard of Hesse-Darmstadt!

Among Liebig's many contributions to the science of nutrition was the concept of nitrogen balance: "All superabundant nitrogen is eliminated from the body as a liquid excrement, through the urinary passages; all solid substances incapable of further transformation pass out by the intestinal canal, and all gaseous matters by the lungs."(3) In 1821 he wrote that, "the nitrogen of flesh and blood, which has been involved in metabolism is found in the urine as urea and uric acid and that the quantity of nitrogen in the urine is directly proportional to the mass of the destroyed organ tissue."

Liebig had also discovered that the carbon and hydrogen in protein that was not needed to form urea and uric acid was eliminated as carbon dioxide and water. He wrote further that "the heat generated by oxidation is entirely sufficient to explain the constant temperature of the body and its loss of heat."(2) Pupils from all over the world traveled to his laboratory in Giessen to learn agricultural chemistry and physiology.

Carl Vogt (1831-1908) (Fig. 7) studied chemistry under Liebig and Pettenkofer. In 1856, he became a faculty member at the University of Munich. In 1863, at the age of 32, he was appointed Director of the Physiological Institute at Munich. Vogt measured nitrogen balance in humans, using Liebig's method of titrating urine to determine its nitrogen content. In 1865 Vogt wrote that the life of the body was the sum of the activity of all the thousands of minute workshops of which it is composed; that a combination of oxygen was not the first step, but that it was a preliminary cleavage of the materials and of simpler materials which, under certain circumstances, might remain unoxidized.

To further investigate these "minute workshops of the body," Vogt and Pettenkofer obtained funding from Maximilian II of Bavaria to construct a calorimeter, which had a room only large enough to hold a bed or a bicycle ergometer. The calorimeter was ventilated with a known volume of outside air. The additional carbonic acid and water measured in the air leaving the calorimeter was the amount eliminated by the subject inside the calorimeter. The quantity of oxygen absorbed by the subject was determined by subtracting the amount of oxygen in the outgoing air from that in the ingoing air.

The calorimeter studies of Vogt and Pettenkofer represent the transition to the modern science of nutrition. In 1881, Vogt wrote, "the mass and capacity of the cells of the body determine the height of the total metabolism. Protein metabolism dictates the direction which it has taken. Protein is a substance which is most readily metabolized, breaking down into materials, one of which is probably fat. The requirement of protein is dependent upon the organized mass of the tissues; the requirement of fat and carbohydrate is dependent upon the amount of mechanical work accomplished."(2)

In 1883-1884 Max Rubner (Fig. 8), who had studied under Vogt, found that carbohydrate and fat were interchangeable in nutrition on the basis of their energy equivalence. This premise is known as Rubner's isodynamic law. Rubner then turned his attention to the caloric value of the excreted constituents of the body, and discovered that one gram of dietary protein oxidized in the body produced 4 calories of heat. He also determined with great accuracy the heat values of various food carbohydrates and fats.

Rubner also studied the mechanism that regulates body temperature and found two factors, the physical and the chemical. The physical regulation of body temperature is accomplished by changes in the distribution of blood to the skin and by the evaporation of water from the skin. The chemical regulation of body temperature operates via changes in the rate of metabolism.

An American student of Liebig's, S.W. Johnson (1830-1909) (Fig. 9), became the first professor of biochemistry in the United States at Yale University in 1856. Another American, W.O. Atwater (1844-1907) (Fig. 10), did graduate work at Yale in 1869 under Johnson. Atwater later became a postdoctoral student of Vogt and a colleague of Rubner.

In 1894 Atwater received an appropriation from the United States Congress to conduct research into human nutrition. His mission included the study of food composition and human food needs. At Wesleyan University, he constructed a calorimeter like that built by Pettenkofer and Vogt (Fig. 11). Atwater studied the biological processes that equate carbohydrate and fat calories and determined the energy equivalents of dietary protein. The Atwater numbers for the energy equivalents of carbohydrate, fat, and protein are used today in the United States; similar numbers calculated by Rubner are still in use in Europe.

In 1895 Atwater compiled a USDA bulletin, "Methods and results of investigations in the chemistry and the economy of foods." In the bulletin he wrote, "Food may be defined as material which when taken into the body serves to either form tissue or yield energy or both. The definition includes all the ordinary food materials, since they both build tissue and yield energy. It includes sugar and starch, because they yield energy and form fatty tissue. It excludes creatin, creatinine, and other so-called nitrogenous extractives of meat... because they neither build tissue nor yield energy. Although they may, at times, be useful aids to nutrition."(4)

In 1897 Atwater reviewed the scientific literature on metabolic investigations. In his view, food consisted of the nutrients protein, fat, carbohydrate, energy, and water. From a biological perspective, the purpose of food was to furnish materials for the building and repair of tissue and to supply fuel for the production of heat and energy. As fuel, food protected the composition of the body from wasting.

When the US Congress had directed Atwater to determine the food needs of the American population, his first reports on food composition in 1892 were measurements of protein, fat, carbohydrate, and energy in the diet. His 1892 data were directly descended from Liebig, in terms of both intellectual heritage and the original development of proximate organic chemical analysis. Only five years later, when Atwater published his review of metabolic investigations, more than 2,299 balance studies in humans had already been reported. Of these studies, 2,234 determined nitrogen balance, and 65, both carbon and nitrogen balance.(5)

Atwater posited that foods were composed of five categories of macronutrients: protein, carbohydrate, fat, energy, and water. This concept resulted in the publication of USDA food analysis tables that included these five nutrient categories. To Atwater, applied nutrition meant the provision of a palatable mixture of foodstuffs arranged in such proportion that the body was burdened with the minimum of labor and the family with the least expense.(6)

Phase II: Micronutrients

In Atwater's era, it was believed that growth would be adequate and health abundant if one analyzed the proximate composition of food stuffs and selected foods appropriate to match these needs. This belief, however, was not substantiated by the facts. One could analyze foods with nearly 100% accuracy, yet could not maintain normal growth and health in animals by feeding them synthetic mixtures of the proximate food substances. Furthermore, the purer these nutrients were, the less successful the synthetic diets in terms of growth. The results from such studies led to a new emphasis: the study of the molecular nature of complex components of food and the body.

In 1906, at Cambridge, Frederick Gowland Hopkins (Fig. 12) was the first to contend that an adequate diet must furnish substances other than proteins, fats, carbohydrates, energy and water. Parallel investigations were begun by Thomas Burr

Osborne and Lafayette Benedict Mendel (1872-1935) (Fig. 13) at Yale and Elmer Verner McCollum (Fig. 14) at the University of Wisconsin and Johns Hopkins.(7) The existence of other "essential" nutrients was hotly contested. The concept was referred to as the "vitamin stunt," because vitamins "seemed to be a figment of the imagination..."(8)

Earlier, Vogt had thought that proximate chemical analysis would not produce a predictable index of food values. Hopkins, Osborne, Mendel, and McCollum all tested the older theory of the "balanced" diet, which assumed that an animal would grow and be healthy if it received an appropriate supply of carbohydrate, fat, and protein, and an adequate total energy intake, all mathematically determined. Their experimental animal studies resulted in the discovery of vitamins, essential amino acids, and trace minerals. All these micronutrients proved "essential" for growth and health, because they could not be produced endogenously, nor could they be supplied by purified diets whose proximate analysis mimicked ordinary diets. These breakthroughs led to a recognition that foods provide fuel, not only for growth and energy, but also for the maintenance of the body's regulatory systems, which enable the processes of life.(7) As a consequence, the list of nutrients in the first U.S. Recommended Dietary Allowances in 1941 included six vitamins, calcium, and iron (Fig. 15).

E.V. McCollum, along with Atwater, Osborne, and Mendel, earned his Ph.D. under Johnson at Yale and later led the discovery of vitamins D and A. In 1957, he summarized his view of nutrition research: "1940 marks the achievement of the primary objectives set by pioneers in the field of [nutrition] study. They sought to discover what, in terms of chemical substances, constituted an adequate diet for man and domestic animals, and that purpose was realized."(9) The finality of his statement seems premature in retrospect, because McCollum did, in fact, lead the way to future nutrition research by teaching that important differences existed between adequate and optimal food intakes.

McCollum believed that health should mean not only freedom from disease, but also the ability to achieve a higher quality of life. Some of the measures of a higher quality of life might include the rate and efficiency of growth in childhood, the time required to reach maturity, the period of full adult capacity and length of life.(7) In *The Science of Nutrition,* published in 1943, Sherman wrote, "there is scientific reason to suppose that heredity is relatively more potent in those cases of *extreme* longevity which seemed to 'run in the family,' in a larger number of families there is not such extreme hereditary trait, and that consciously cultivated, nutritionally guided, good habits as to what foods one eats and in what proportions may very probably be the greatest constructive influence contributing to higher health and longer life. Whatever one's original chromosomal endowment and whether his hereditary background is favorable, he still, as a reasonably normal member of a mammalian species, influences through his food and nutrition [the] development of innate potentialities, either for the better or for the worse."(7) These views presaged the subsequent era of nutrition research.

The search for additional trace factors to account for improved biological function continued in more and more laboratories. The impact of these investigations (Fig. 15) was reflected in the expansion of the number of nutrients listed in the U.S. Recommended Dietary Allowances. In 1968, vitamin E, folacin, vitamin B_6, vitamin B_{12}, phosphorus, iodine, and magnesium were added to the list, in 1974, zinc, and in 1989, vitamin K and selenium. These additions brought to a total of 20 the number of nutrients in the Recommended Dietary Allowances made by the U.S. National Academy of Sciences.

In 1975, the USDA publication, *Composition of Foods* (Agriculture Handbook No. 8) received attention paralleling that of the Recommended Dietary Allowances. In the 1975 edition, energy, protein, and fat were determined for approximately 2,500 foods. In the food composition tables, carbohydrate was subdivided into total and fiber; the other nutrients identified for each food item included water, food energy, protein, fat, total ash, calcium, phosphorus, iron, sodium, potassium, vitamin A, thiamin, riboflavin, niacin, and ascorbic acid. In the next edition of Handbook No. 8 (in the mid 1980s), the numbers increased for both analyzed nutrients and foods; nearly 80 nutrients were analyzed from over 6,000 foods. New to the nutrient list were zinc, copper, manganese, pantothenic acid, folacin, and vitamins B_6 and B_{12}. In addition to total fat, fatty acids (reported by chain length and saturation), cholesterol, and phytosterols were listed, and the analysis of 18 amino acids was included.

Phase III: Molecular Nutrition

As research into nutrients and their effects became more complex, a major difficulty was the investigation of the chemical reactions within the living body. Both food and living tissues are made up of protein, fat, and carbohydrate, and in these early investigations, when the food products liberated by digestion were absorbed, they merged with identical molecules that originated from degradation in tissues. The accumulated knowledge of intermediary metabolism, therefore, was a result of external "balance" experiments in which the intake and the losses were tabulated. Carbon oxidation was viewed as heat produced in the thousands of structured workshops of the body.

A new opportunity for understanding metabolic processes developed after Harold Urey discovered heavy hydrogen and devised methods to isolate heavy isotopes of carbon, nitrogen, oxygen, and sulphur. Rudolph Schoenheimer (Fig. 16) was able to use these materials in his precedent-setting investigations of metabolism, because the living organism does not discriminate between isotope tracers of the same element. In the technique established by Schoenheimer, the food nutrient or organ to be investigated is labeled so that the heavy isotopic composition of its constituent atoms can be identified. After feeding an isotope-labeled nutrient to an animal or living cell culture, other compounds that contain the isotope are isolated. The presence of the tracer is an indication that a precursor molecule has been converted in vivo to another product.

The dynamic interactions of food and tissue molecules observed using these techniques have led to a new understanding of the nutritional process, a shift from trace nutrients to tracer nutrient metabolism. We have learned, for instance, that when fat is absorbed, the fatty acids of dietary origin merge with those from the lipid depots, thereby forming a pool in which the origin of the fatty acids is indistinguishable. Some are degraded, and some reenter ester linkages to regenerate fat, which is transported back to the depots. In normal subjects, these reactions are balanced such that both the total amount and the structure of fat in depot, blood, and lean tissues remain constant. In obese subjects, however, there is a reduction in the oxidation of dietary fat accompanied by an increase in fat storage.(11)

As another example of our better understanding of the nutritional process, we now know that the replacement of the amino acids of tissue proteins and the transference of nitrogen involves the rapid turnover of tissue proteins. Although the peptide bonds are essential parts of the proteins, they are rapidly and continually turning over in all normal animals. Furthermore, synthesis of nonessential amino acids, like that of fatty acids, proceeds even when there is no obvious need for them.

Further, the ability to label molecules of food has led to the understanding that the dynamic chemical reactions in the nutritional process are balanced so delicately that the body components remain constant. This constancy is not, however, an indication that the structural framework of the living organism is inactive and takes little part in metabolism. As Atwater had predicted, amino and fatty acids play a dual role: the replacement of cellular structural elements and the maintenance of specific cellular chemical reactions. The macromolecules are under the influence of hydrolytic enzymes, constantly being degraded. These degenerative changes are balanced by synthetic processes, which must be coupled to other biochemical reactions, such as mitochondrial carbon oxidation or receptor dephosphorylation.

The macromolecules in living matter require for their maintenance the steady occurrence of an abundance of enzymatic reactions. The discovery of rapid cellular molecular regeneration, involving a constant transfer of specific groups, suggests that the biological system represents a great cycle of closely linked chemical reactions. This idea, however, can scarcely be reconciled with Atwater's comparison of the living being to a combustion engine or his theory of independent structure and metabolism. The new results imply that not only the fuel but also the molecular units from tissues and foods are in a steady state of flux. The classical picture must thus be replaced by one that takes account of the dynamic state of molecular body structure.(11)

The most important function of the new heavy isotope methodology is its ability to trace the passage of the molecular nitrogen and carbon previously identified by proximate analysis in balance study. The work in humans began in 1961 when Waterlow (Fig. 17) determined the turnover of in N_{15}-labeled glycine in malnourished children. The studies of subsequent investigators have revealed that the rate of whole body protein synthesis is approximately 4 times greater than that suggested by the net "balance" retention of body nitrogen.(12)

The uniform labeling of foods with heavy isotopes presents a unique opportunity to determine the essentiality and fate of molecules from foods (Fig. 18). The carbon or nitrogen is uniformly marked in the diet and easily distinguished from the unmarked nonessential molecules synthesized by the body. This technique enables us to determine which nutrients have a genetic dietary requirement (the essential nutrients) and which are synthesized by genetically expressed enzymes within the body (the semi- and nonessential nutrients). In addition, we can measure changes in the synthesis of genetically conditional amino acids that result from growth or metabolic stress.(13)

The use of heavy isotopes has led to the discovery that some food macromolecules can be absorbed intact and utilized as if they had been produced in the body. For example, a preterm infant absorbs lactoferrin (Fig. 19) intact from his or her mother's milk. This finding and the fact that a preterm infant has less ability to synthesize lactoferrin suggest that lactoferrin could be classified as a nutrient beneficial for such infants. Although many infants who are fed cow's-milk formulas grow and develop normally without maternal lactoferrin, the infant who is fed maternal milk has a better immune function than the infant who is fed formula.(14)

The results from this type of research have led us to recognize (Fig. 20) that food has yet another function: to provide messages that modulate the animal's metabolism. Such messages might modulate growth or differentiation, or the activate other messenger systems within susceptible tissues. The future Recommended Dietary Allowances will probably expand the list of molecular nutrients, and the future USDA food composition publications will reflect food requirements classified by specific human genetic variables.

Table. Nutrients Listed in the Various Editions of the U.S. Recommended Daily Allowances

					Vitamins															
Year	Calories	Protein	Ca	Fe	A	B_1	B_2	B_3	C	D	E	K	Folacin	B_6	B_{12}	Phosphorus	Iodine	Mg	Zinc	Se
1941	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓										
1943	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓										
1945	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓										
1948	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓										
1953	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓										
1958	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓										
1963	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓										
1968	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓		
1974	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	
1980	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	
1989	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓

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