

# Nutrition Research . . . . .

## Potentialities in Chronic Disease

By WILLIAM H. SEBRELL, Jr., M.D.

**H**EALTH MAINTENANCE and constructive medicine—two emerging concepts in modern public health—weigh heavily in any consideration of nutrition in light of our aging population and the increasing significance of chronic disease.

We have made great strides against deficiency diseases, such as pellagra, beriberi, rickets, and goiter. While performing our day-to-day task of maintaining and extending these advances, we can now think in terms of constructive or optimum nutrition, with its implications for promoting healthful, productive longevity.

Aging, nutrition, and public health are directly related in various ways. Special feeding problems and nutritional needs of old people are of primary concern, and nutrition problems are common in the treatment of chronic diseases, for example, when digestion is impaired. Closely related is therapy by dietary means, as in diabetes and gout. An-

other—and fundamental—aspect is chronic disease research, a major objective of which is a better understanding of metabolism.

In much of this effort, primary attention is given to the complex interrelation of nutrients with enzymes, hormones, and other metabolic agents. Encouraging progress has been made, but our knowledge is still fragmentary and requires much supplementation. In other research not directly concerned with nutrition, knowledge and techniques are being developed that can be readily applied in the nutrition field.

### Obesity and Chronic Disease

An important but little understood link between nutrition and chronic disease is obesity—a major problem called sharply to attention by actuarial experience, and now being investigated in several laboratories. About a quarter of the adult population is sufficiently overweight to impair health.

No better understood than the role of obesity in disease is the relation between obesity and the aging process. As we pass through the middle years, the percentage of body fat usually rises, though the overall weight may remain the same. Thus, among groups of standard weight, fat may comprise only 10 percent of the body weight in younger men, as compared with 21 percent in older ones. The prevalence of obesity increases to about age 40 for men and 50 for women, and declines after age 60. This decline is due not only to loss of fat, but also to the loss of fat people.

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*Dr. Sebrell is director of the National Institutes of Health, Public Health Service. On June 22, 1953, he spoke before the Institute of Food Technologists at its 13th annual meeting in Boston on "The changing age pattern of the American population, with its implications in the field of public health." This is a portion of his paper—that dealing with metabolic investigations related to chronic diseases. The full text, with citations, is scheduled for publication in Food Technology for September under the title of "Aging, Nutrition, and Public Health."*

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*The wee son turned the shining future up;  
His father plowed the green past under.*

—From *Man and Boy*, by Alma Robison Higbee



**Dr. Goldberger and Dr. Sebrell**

The Joseph Goldberger Award in Clinical Nutrition is presented by the Board of Trustees of the American Medical Association for outstanding and sustained work in the field of clinical nutrition. The 1952 award, which includes a gold medal and a check for \$1,000, made possible by a grant from the Nutrition Foundation, was given in December to Dr. William H. Sebrell, Jr., Assistant Surgeon General of the Public Health Service and Director of its National Institutes of Health. He was selected because of his outstanding work in the field of riboflavin deficiency, in pellagra prevention with Dr. Goldberger, and for his continued work in the field of clinical nutrition. The previous recipients of the award were Dr. Randolph West and Dr. Fuller Albright. In response to the presentation of the award, Dr. Sebrell discussed the present status and the future of nutrition as it relates to medicine in America. His remarks were published in the *Journal of the American Medical Association*, May 2, 1953, pp. 42-44.

On pages 737-746 are two recent papers by Dr. Sebrell—one dealing with nutrition research, the other with public health aspects.

**J**OSEPH GOLDBERGER'S life (1874 to 1929) "was a Horatio Alger experience common to other great Americans. He was born on a peasant tenant farm in Czechoslovakia in 1874 and brought to New York City when he was 7," according to Williams (p. 279, *The United States Public Health Service, 1798-1950*). "For the early part of his life he delivered groceries for his father on the lower East Side. At 16, he decided on a course of civil engineering, but 2 years later switched to medicine after he heard the Harvey Lecture given by a Bellevue Hospital College physician. In 1895 he graduated second in his class at Bellevue, where he had acquired a reputation as a hater of routine but a master of case history writing. To him every case was a great and absorbing mystery, the solution an exciting challenge. After a 2-year try he decided that private practice was not his field and he entered the Marine Hospital Service. He performed brilliant and dangerous work on typhus fever, operating always at the epidemic scene. He also made important studies of the Mexican form of typhus fever and of yellow fever. But the chance to exercise his talents, his greatest contribution to humanity, came when he was put in charge of pellagra investigations."

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The fact that obesity is correlated with aging and chronic disease does not in itself imply a causal relation. Unknown etiological factors may be common to these conditions. In various studies, however, caloric restriction has prevented cancer in mice, prolonged greatly the life of rats, and reduced the signs of diabetes in humans. Moreover, striking decreases in the incidence and severity of diabetes and hypertension accompanied undernutrition and loss of weight in certain European countries during both World Wars. It may reasonably be assumed then that practical advances against obesity would have far-reaching effects upon public health.

This problem is fertile for research. We should like to know, for example, what benefits in longevity accrue to the middle-aged person who reduces and maintains the reduction. We need clarification of the mechanism, psychological or metabolic, that leads to overeating.

Wading through the wilderness of conflicting theories as to the cause of pellagra, and in the face of those who claimed to have proved that it was infectious in origin, Goldberger's first theory, which he announced in 1914, was that pellagra was due to a deficiency in diet. This he proceeded to prove conclusively and devised ways in which the disease could be prevented and cured. Even so, he did not discard the possibility that pellagra might have an infectious element until he proved to his own satisfaction that this could not be true. This he did by injecting blood from patients with pellagra into himself, his associates, and even into his own wife. Furthermore, he made pills from the intestinal discharges and the skin rash scales from pellagrous subjects and ate them as further proof that no infectious agent was involved.

Later he sharpened his ideas about the dietary origin of pellagra to include the concept that a "vitamine" deficiency was involved. This was a quite new concept in disease etiology since Funk had coined the name "vitamine" only in 1911. Later his ideas shifted to include the possibility that an amino acid deficiency, specifically cystine and tryptophan, was causative. Both of these theories were proved after Goldberger's untimely

death, although it was not until 1945 that the amino acid tryptophan was clearly implicated.

Never one to form a theory and fail to test it, Goldberger and his associates reported in 1922 on tests with cystine and tryptophan, although their claims for therapeutic value were very conservative. For reasons unknown, he never reported on some dramatic results which he and his associate Tanner obtained with tryptophan alone. Nicotinic acid was not known as a vitamin during his lifetime so it could not be tested.

Goldberger's influence on nutrition research continued long after his death and continues even today. The dog, which he introduced and established as a tool in pellagra research, is still used today. The dietary data which he and his associates collected have been used recently to recalculate the human requirement for nicotinic acid.

Not the least of his amazing abilities was his capacity to gather brilliant associates who ably continued the work after his death. His career in research was marked by courage, rare intellectual insight, wisdom, and perseverance. In the words of Dr. Arthur M. Stimson: "He illuminated everything he touched and won the admiration and affection of his associates."

—JAMES M. HUNDLEY, M.D.

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We should define the role of heredity—a primary factor in the obesity of certain strains of mice. And we may hope that such knowledge will improve means for controlling obesity through public health programs.

#### **Fat Metabolism and Atherosclerosis**

This subject of obesity provides a point of transition to the role of fat metabolism in the development of cardiovascular diseases. Among these is atherosclerosis, the most serious form of hardening of the arteries, which causes 9 out of 10 heart attacks and seriously disables hundreds of thousands of persons. This is a type of arteriosclerosis in which the lining of the artery thickens and pushes inward. Deposited cholesterol, a fatlike substance, is a part of this growth.

Observations on patients following weight reduction have shown a decline in circulating cholesterol of the type suspected in atherosclerosis. To what extent the lower cholesterol level

is due to reduced fat ingestion rather than reduction of weight has not been determined.

Research on atherosclerosis is proceeding along many lines. Most investigators, however, work from the hypothesis that the body's fat-handling system plays a part in the development of the disease. Not only have abnormal cholesterol-bearing molecules been found in the blood of sclerotic patients, but some animals on high cholesterol diets develop sclerotic lesions.

Investigators at the National Institutes of Health recently identified a "clearing factor," which diminishes the cloudiness of blood occurring after a fatty meal. In normal persons this condition clears automatically within a few hours, but in others it persists, possibly leading to atherosclerosis. The clearing factor not only eliminates the cloudiness, but appears to break down the abnormal cholesterol-bearing molecules that are particularly suspect.

The fact, however, that the body readily

synthesizes cholesterol from simple, ever-present substances compels caution. Moreover, we do not yet know whether the dietary level of the substance is of practical significance. Cholesterol metabolism involves such nutrients as choline, other B vitamins, and some amino acids; and various nutritional deficiencies affect the deposition. For persons with atherosclerosis, the best diet known at present is a balanced one, such as normal people require. If other problems, such as hypertension, are involved, a special diet may be indicated.

### **Cancer and Nutrition**

Cancer is another chronic disease in which the science of nutrition is contributing valuable information. Dietary manipulations have been shown to exert pronounced effects on cancer causation in animals. Caloric restriction prevents or delays the appearance of various tumors; and restriction of certain amino acids gives similar results. Choline deficiency, on the other hand, induces liver cancer in the rat. These observations have no immediate practical value, since the preventive diets abolish breeding capacity and choline occurs in a wide variety of foods. Such findings, however, are important leads for further research.

In human beings, cancers already established have shown little response to dietary alternations; but in animal experiments, alternate restriction and supply of a vitamin, such as riboflavin or pantothenic acid, has appreciably prolonged life. Vitamin antagonists have produced similar effects: in some children, chemical antagonists to folic acid, such as aminopterin, have been of temporary benefit in leukemia. Recent advances in leukemia concern certain pyrimidine compounds. When administered to animals, these drugs in combination with a folic acid antagonist appear to inhibit neoplastic growth more than antifolics alone. For nutritionists, the exploration of such antimetabolites offers rich opportunities for extending knowledge of normal and abnormal growth.

### **Bone and Joint Diseases**

The study of arthritis, the principal crippling disease, has been hampered by lack of a method for producing the disease in experimental animals. Recently, however, several investi-

gators have produced arthritic changes by dietary means.

At Washington University in St. Louis, a condition resembling osteoarthritis was induced in mice of a highly inbred strain. A high fat diet was fed to one group, a high protein diet to another. The mice that received the fat-enriched diet showed an acceleration of skeletal aging and an increased incidence of osteoarthritis, whereas protein enrichment retarded aging of the joints and delayed the onset of joint disease.

Other groups of workers, one at Kansas City College and another at Cambridge University, report a disease in vitamin-C-deficient guinea pigs that resembles rheumatoid arthritis. It is interesting that these joint changes can be prevented with cortisone.

A recent advance now being applied clinically concerns osteoporosis, a brittle condition of the bones due to decalcification. It is primarily a disease of the aged, but may occur at any age as a late phase of arthritis. At the Russell Sage Institute of Pathology, osteoporosis is being treated successfully with the metal strontium. After maximum calcium storage, strontium can still be stored in the bones. Maximum retention of both minerals is achieved with the aid of auxiliary agents—vitamin D and sex hormones. This, as well as the fact that osteoporosis often results from ovarian insufficiency, clearly suggests a relation between nutrition and hormones for which we have no explanation.

Nutrition science, using new biochemical approaches, offers much promise against diseases of the bones and joints. Even the study of an inorganic nutrient such as calcium presents attractive possibilities. The skeleton is now regarded as a living tissue, particularly in view of tracer studies showing that calcium enters and leaves the skeleton with considerable rapidity. Little is known, however, about the regulation of calcium metabolism. How, for example, is calcium mobilized to the area of a tuberculous lesion? In leprosy, though a bacterial disease, why do entire bones sometimes disappear as a result of resorption? Explanations of such metabolic disturbances could aid in the prevention of arthritic deformity.

### Research for Optimum Nutrition

Nutrition science has made great strides in the past, but the opportunities for further progress are limitless. Long-term investments in fundamental research represent an approach historically proved to offer the best returns in the long run. There is a constant exchange, of course, between basic and applied science. Research in nutrition, applied as well as fundamental, will help workers throughout the world in promoting health and long life.

A constructive approach requires that we strive to attain, and to maintain, optimum health while repairing damage. Fortunately, the population as a whole has lost much of its complacency concerning nutrition. Food technology, through food fortification, increased availability and palatability of foods, and other innovations, is a major aspect of the public health approach through which the need for

specific nutritional therapy may some day be eliminated. The human body is remarkably adaptable, and inherent abnormalities of digestion and metabolism may lead to compensatory dietary practices. Unfortunately, however, the contrary is frequently the case; selection and consumption of food often obey a misleading appetite, and the result may be damage and disease.

Nutrition science is only beginning its venture into gerontology and the major chronic diseases. Whether substantial contributions are achieved in the near future depends largely on the cooperative efforts of many individuals and groups. No longer is scientific progress by lone investigators the rule, as in the days of Pasteur and Ehrlich. Many disciplines must coordinate their attack. Nutrition research and theory must be converted to food therapy, nutrition knowledge, to public health gains.

## *Enrichment . . . . .*

# a Public Health Approach to Better Nutrition

By WILLIAM H. SEBRELL, Jr., M.D.

WE ARE inclined in these modern times to take our knowledge of nutrition for granted and to underestimate the importance of its application. Consider for a moment the problem of malnutrition in earlier days. Vasco de Gama, in his search for a water route to the East, rounded the Cape of Good Hope and returned with only a third of his crew, the rest having died of scurvy. At one time the channel fleet of the British Navy could not be manned because of the prevalence of scurvy among the crews. In the late 19th century, 40 percent of the seamen in the Japanese Navy died of beriberi; and in Italy at about the same time, the reported cases of pellagra exceeded 104,000. One by one, these and other serious diseases re-

sulting from specific dietary deficiencies have yielded to science.

The progress of nutrition research, however,

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*Dr. Sebrell presented this paper at Toronto on January 26, 1953, as Canada inaugurated a program of flour and bread enrichment. Speaking before the First Nutrition and Enrichment Conference of the Baking and Milling Industries, he characterized the Canadian enrichment program as "one more forceful blow in the prevention of malnutrition . . . further indication of the increasing role of enrichment in the health and strength of nations." His discussion, here somewhat condensed, appears in full in The Canadian Hospital for June 1953.*

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