In 1967 the Food and Nutrition Section celebrated its 50th anniversary. For this occasion a symposium was organized to review 50 years of experience in nutrition and to take a look at the future. Four notable pioneers in nutrition presented their views, and they are offered here to the readers of the Journal. To praise these contributions would be to gild the lily.

FIFTY YEARS OF EXPERIENCE IN NUTRITION AND A LOOK TO THE FUTURE

I. FOODS AND NUTRITION THROUGH FIFTY YEARS

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Fifty Years Ago

PERHAPS an ideal concept for celebrating a Golden Anniversary is to review the past 50 years and then to challenge our vision of what to strive for during the next 50 years. By coincidence it was just 50 years ago, almost to a day, in 1917, when I first heard of the mysterious things called "vitamines," while a student at Washington State College. Literary societies were an important part of college life in those days. No dances were permitted except on Saturday evenings, but cultural activities such as literary societies were permitted on Friday evenings. At one of these meetings a senior in agriculture gave a really exciting talk on the work of Lunin, Eijkman, Hopkins, McCollum, Osborne, and Mendel. He impressed all of us by his declaration that evidently all of our food and feed supplies would have to be restudied, both on a chemical and on a biological basis, and this was going to take a long time. How right he

tion chemist, trained at the University of Wisconsin, asked me to prepare a demonstration of vitamin-deficient albino rats for their annual extension course for farmers. The rat demonstration was sheer joy compared to the next assignment. In a small room with hoods that did not function very well, I had to digest several dozen thyroid glands from sheep, in fused sodium hydroxide over Bunsen burners, as a first step in iodine analysis. The fumes repeatedly drove me out of the laboratory, thoroughly nauseated. However, this experience had an intense personal interest because it marked the turning point in solving the goiter problem in my home community in the Columbia River Valley. The incidence of human goiter was very high, including my older sister and many neighbors, and among livestock there was a serious problem of big necked sheep, hairless pigs, and weak or stillborn colts and calves. The animal problem was solved quickly, but the human one moved much more slowly.

Although Professor Matthews, then at the University of Cincinnati, was not

so widely known as others for his research accomplishments, his textbook made a great contribution to inspired teaching in nutrition and biochemistry, through two decades. It was *the* standard text in nearly all medical schools and in other courses in biochemistry. His few pages on vitamins at the end of the book made a very strong impression on many of us. When I mentioned to my rather conservative professor in the spring of 1918 that I thought vitamin studies would be a good field for research, he expressed serious doubt, saying "If you were going to live in China or in the Philippines it might be all right, but that field is not likely to be an important one in the United States where we have a good food supply."

More surprising was the advice given in 1930 to the graduate student, William Waugh, who finally isolated vitamin C in our laboratory at the University of Pittsburgh. When he told his previous employer that he planned to work with me on the vitamin problem for his Ph.D. thesis, the physician replied, "If you want to work with Professor King, that's fine, but don't work on the vitamin problem; chemists all over the world have been working in that area for twenty years and no one has found one yet."

Some of the journals that year had published suggestions that it was futile to attempt isolation of the vitamins because they were simply activated material that lost its function when prepared in crystalline form.

Two very important public health campaigns were under way in 1917, based directly on nutrition. Marine, Kimball, Hart, Smith, and others in the Middle West were accumulating evidence to support the addition of iodine to salt to prevent goiter in man and in animals; and in New York City, Alfred Hess was waging a campaign against the high incidence of scurvy. Dr. Hess and others had pioneered with resounding success in support of milk pasteurization, and achieved a sharp drop in the sickness and death rates among children from so-called "summer complaint"; but unfortunately, there was a parallel rise in the incidence of scurvy. The latter was caused by the contamination of the milk with traces of copper from commercial pasteurizing equipment, which catalyzed oxidation of the vitamin. Under the vigorous guidance of Dr. Hess, this problem was solved fairly quickly in cooperation with the dairy industry. He published three papers on infantile scurvy in 1917 and nine more within the next three years, followed in 1920 by his classical book, "Scurvy: Past and Present." Dr. Hess was also an outstanding pioneer in clinical research on vitamin D and rickets.

Pittsburgh Days

After initiating a modest program on the molecular structure of fats at the University of Pittsburgh, I had the good fortune to be granted a year's leave of absence to study with Professsor H. C. Sherman at Columbia University. At that time I decided to undertake a second area of research directed toward the characterization and possible isolation of vitamin C, in cooperation with graduate students. This area of research was chosen primarily to afford student training in chemistry that had a direct element of animal experimentation. The first student to start with me in the new venture was Horace L. Sipple, executive secretary of the Nutrition Foundation, and a very active member of our Section of the American Public Health Association. Not in complaint, but as a reflection on academic practices at that time, my teaching schedule included courses in inorganic, organic, food and sanitation, industrial and advanced biochemistry, with a total of 20-23 classroom hours per week.

So far as we knew at the time, in 1927, the only two persons working toward identification of vitamin C were S. S. Zilva in London, and N. Bezssnoff in Paris. The status of other vitamins was being studied very actively, but there was still uncertainty about the identity of vitamins A, B_1, and D, and "B_2" was still a mysterious package represented in bioassay diets for other vitamins as "4 per cent by weight of autoclaved dry brewers yeast."

In the late summer of 1931, Mr. Waugh began to get crystalline preparations with uniform biological value. After rechecking the work carefully through a second purification as the lead salt, we published our data in the spring of 1932 and continued to study the vitamin's functional role as a single compound, with one active reversibly oxidized form. In view of the multiple nature of the original vitamins, A, B, and D, we were fortunate in choosing vitamin C for identification. The sensitivity to oxidation and the standard 90-day assay period were major handicaps in that area of research. In later studies, after World War II when radiocarbon became available, we were primarily interested in discovering the precursor of vitamin C, which proved to be D-glucose, through the intermediate formation of D-glucuronic acid and L-guluronic acid lactone, with end products chiefly carbon dioxide and oxalic acid.

Professor Sherman and Columbia

Professor Sherman encouraged others to work on the chemistry of vitamins and their various functions, but he held closely to the areas where he believed he could make the greatest contributions, namely (a) in developing assay procedures so that the nutrients could be dealt with quantitatively, and (b) in quantitative feeding experiments to establish health relationships on a life span basis. He was fond of saying that rats and guinea pigs were his balances and burettes. In these fields, in teaching, and in writing textbooks of outstanding merit, he was one of our greatest leaders. His cooperation with Mary Swartz Rose and her associates in Teachers College was an important factor in both teaching and research.

The amylase enzymes also held Professor Sherman's interest through many years, in association with Dr. M. L. Caldwell. His work on the essential protein nature of the enzyme, pancreatic amylase, stood out as one of the sharpest challenges to Professor Willstatter's claim that many of the purest enzymes did not contain protein. With Professor Sherman seated in front of him, Dr. Willstatter persisted in his claims, during his 1927 lectures in New York, even though Dr. Sherman had pointed out the experimental error in his work very clearly in published papers. It rested on two very simple points, namely, that the enzyme activity test was far more sensitive than the protein test used, and second, that the test for protein was made after a long period of dialysis which permitted hydrolysis of much of the protein originally present. Many persons will recall that there was a similar hesitancy, lasting through many years among European chemists, to accept the classical protein-enzyme reports of Dr. J. B. Sumner and Dr. J. Northrop. The tide turned, however, when the latter two men received a Nobel Prize.

Since many of the leading research groups during the early years of the period under review are not represented by speakers on the program, it was suggested that each of us on the program should cover briefly the work of several scientists beyond those with whom we worked directly.

Cambridge and Wisconsin

A half-year at Cambridge University in 1929 to work in Professor F. G. Hop-

kins' laboratories was greatly enjoyed. Although I completed a paper on enzyme studies of liver esterase, and continued work in that field after returning to Pittsburgh, the most valuable discovery at Cambridge was to find Professor Conrad A. Elvehjem there. His chief enjoyment at Cambridge was in working with Professor Keilin in microrespirometry. His background in iron and copper research intensified their mutual interest in exploring the cytochrome system of respiration. He resolved to bring back to Wisconsin a Warburg-Barcroft type of equipment even if he had to pay for it himself.

We both agreed that enzyme research, as a major field in biochemistry, had been relatively neglected in the United States. Twice after his return he asked me, and I imagine others as well, to send a special memorandum in support of his drive to build up a strong enzyme research center at the university. Not long after the second request, he said "I think we are going to have an Enzyme Research Institute."

Through the interest of Professors McCollum and Neil Gordon at Johns Hopkins, we arranged a special program at the Gibson Island conferences (forerunner of the AAAS Gordon Conferences) to deal chiefly with the respiratory enzyme systems and related equipment.

The nicotinic acid work at Wisconsin will be covered by Dr. Sebrell in his paper. Time does not permit a summary of the remarkable series of research papers from the University of Wisconsin dealing with other vitamin and mineral studies, tissue respiration, dental caries, nutritional pathology, nutrition and carcinogenesis, and the broad field of intermediate metabolism. However, one cannot omit mention of the notable work of such scientists as Babcock, McCollum, Steenbock, Hart, Peterson, Fred, Parsons, and Phillips.

Cornell University

The contributions from Cornell University should have much greater recognition than is possible to include in today's program. A large part of the research and teaching on the Ithaca campus has been guided by Professor L. A. Maynard. The research on mineral metabolism, vitamins, soil-plant-and-animal relationships, lactation, efficiency of feed utilization and energy studies have added steadily to knowledge in both human and animal nutrition. Professor Clive McCay's pioneering animal studies in demonstrating the handicap to survival that is imposed by ad libitum feeding of animals has had an increasing significance in human experience. At the Cornell Medical Center in New York, the research record is one of continuing brilliance under the leadership of Graham Lusk, Stanley Benedict, E. F. Dubois, and Vincent Du Vigneaud.

Individual Citations

The pioneering work of Robert R. Williams will be reviewed later in Dr. Sebrell's paper, but I must mention the many basic contributions of his brother Roger Williams, particularly in relation to pantothenic acid, folic acid, and biological variations in metabolic patterns.

Although not in the United States at the beginning of his career, Dr. Paul Gyorgy was one of the key contributors to research in relation to riboflavin, pyridoxine, biotin, and finally in relation to proteins.

A Fiftieth Anniversary record must also include citation of our greatest pioneers in research and in training personnel in relation to carbohydrate aspects of nutrition: Sir Frederick Banting, Charles H. Best, A. Baird Hastings, John R. Murlin, and the famous team of Carl and Gerty Cori.

At the University of Rochester, Dr. Walter Bloor and Karl Mason were out-

standing in research on lipid metabolism, working in parallel with H. J. Deuel, Jr., at the University of Southern California. Calorimetry was at its height under the leadership of Francis Benedict, W. 0. Atwater, E. F. Dubois, Graham Lusk, H. F. Armsby, and E. B. Forbes.

Other famous groups included H. M. Evans, Agnes Fay Morgan, H. J. Aimquist, and Samuel Lepkovsky at the University of California; L. S. Palmer, Ross A. Gortner, and George Burr at the University of Minnesota; Walter Cannon, Otto Folin, S. B. Wolbach, H. C. Stuart, Bertha Burke, and George Wald at Harvard University; Icie Macy Hoobler and Helen Huncher at the Children's Fund of Michigan; Lydia Roberts and Paul Cannon at the University of Chicago; E. B. Forbes, R. Adams Butcher, H. P. Armsby, and N. B. Guerrant at Pennsylvania State College; Edward Doisy at St. Louis University; H. B. Lewis at the University of Michigan; Glen Cullen, J. Warkany, Tom Spies and their associates at Cincinnati; L. Emmett Holt, Jr.? at Johns Hopkins and New York University; John Youmans at Vanderbilt; D. B. Jones and Paul E. Howe in the Department of Agriculture, and many others that should be mentioned if time permitted.

Although we have witnessed far greater progress in nutritional knowledge during the past fifty years than had been accomplished in all previous history, the horizon is still crowded with questions and challenges that we are obliged to meet.

We can only feel very humble when we see how inadequately we are finding solutions to the world-wide need for nutrition that will permit normal health or even survival among millions and millions of children. In many sections of Latin America, Africa, India, and Southeast Asia, stark malnutrition is already one of the greatest causes of sickness and death, and the risk is obvious that the situation may get worse before it gets better. In the forefront of problems beyond increasing the production of foods of high nutritive quality, is the difficult task of research to find how extensive are the irreversible injuries to the central nervous system imposed by malnutrition among very small children. The degree of physical stunting, sickness, and death resulting from malnutrition is becoming obvious, but the degree of permanent damage to the nervous system is far more difficult to evaluate. Efforts in this direction are still pitifully small.

Another problem has had almost no attention, namely, the nutritional state of our greatest leaders in government and in other aspects of civic life when they are making the great decisions that are crucial for the welfare of all mankind, nationally and internationally. We constantly see the practice of such groups and individuals working far into the night or early morning with little or no nourishment and further handicapped by the consumption of tobacco and alcohol—echoes of "the smoke-filled room" so familiar in political life. Their intellectual efficiency might well be challenged on physiological grounds. I admit, however, that it would be difficult to design the technics for experimental and control groups.

We are almost as far from solving the nutritional problems among well-to-do populations. To start with, we have no comprehension of the genetic or early-in-life trends among our own or other populations in relation to the metabolic diseases such as diabetes, atherosclerosis, hypertension, heart attacks, strokes, and other breaks in health that beset those in the upper half of the age span. Neither do we understand the interplay between nutrition and social or psychological tensions that tend to distort the personality of so many people. Hence, nutritional measures to counterbalance such trends early in life are neither identified nor applied early

enough to be effective. A lifespan concept of optimum nutrition for each individual is a goal we should be searching for, even though it now appears to be far in the future.

ACKNOWLEDGMENT—We are indebted to Dr. Juanita Eagles and Miss Helen Ger Olson for their very substantial accomplishment in preparing an interesting and remarkably complete history of our Section, and to Dr. Robert Shank for arranging this program.

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This paper was presented before a Joint Session of the National Dairy Council and the Food and Nutrition Section of the American Public Health Association at the Ninety-Fifth Annual Meeting in Miami Beach, Fla., October 23, 1967.

Official Monthly Publication of the American Public Health Association, Inc.

AMERICAN

Journal of Public Health

AND THE NATION'S HEALTH

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VOL. 58, NO. 11

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