mine the positions of the other two disulfide bonds by means of enzymic hydrolysis, since no enzyme would split between the two consecutive half-cystine residues of the A chain. It was therefore necessary to reinvestigate the possibility of using acid hydrolysis.

The disulfide interchange reaction that occurred in acid solution was found to be different from that occurring in neutral and alkaline solution and instead of being catalyzed by —SH compounds was actually inhibited by them. This not only showed that a different reaction was involved but it also made it possible to prevent its occurring during acid hydrolysis. Thus, when insulin was treated with concentrated acid to which a small amount of thioglycolic acid was added, cystine peptides could be isolated which were in fact true breakdown products and from which the distribution of the remaining two disulfide bonds could be deduced. These are shown in Fig. 2, which shows the complete structure of insulin.

Of the various theories concerned with protein chemistry, our results supported only the classical peptide hypothesis of Hofmeister and Fischer. The fact that all our results could be explained on this theory added further proof, if any were necessary, of its validity. The results also showed that proteins are definite chemical substances possessing a unique structure in which each position in the chain is occupied by one, and only one, amino acid residue.

Examination of the sequences of the two chains reveals no evidence of periodicity of any kind, nor does there seem to be any basic principle which determines the arrangement of the residues. They seem to be put together in an order that is random, but nevertheless unique and most significant, since on it must depend the important physiological action of the hormone.

Biological Activity and Chemical Structure

As yet little is known about the relationship of the physiological action of insulin to its chemical structure. One approach to this problem was to study the insulins from different animal species (*16*). Since all insulins show the same activity, it could be concluded that differences would be found only in parts of the molecule that were not important for activity.

All the results given above were obtained on insulin from cattle. When insulins from four other species were studied by essentially the same methods, it was found that the whole of the B chain was identical in all species, and the only differences that were found in the three amino acids contained within the disulfide ring of the A chain, which in the cattle are

Ala-Ser-Val

and in the other species are as follows:

Pig, Thr-Ser-Ileu
Sheep, Ala-Gly-Val
Horse, Thr-Gly-Ileu
Whale, Thr-Ser-Ileu

These results suggest that the exact structure of the residues in this position is not important for biological activity, but it does not follow that the whole of the rest of the molecule is important.

The determination of the structure of insulin clearly opens up the way to similar studies on other proteins, and already such studies are going on in a number of laboratories. These studies are aimed at determining the exact chemical structure of the many proteins that go to make up living matter and hence at understanding how these proteins perform their specific functions on which the processes of life depend. One may also hope that studies on proteins may reveal changes that take place in disease, and that our efforts may be of more practical use to humanity.

References

1. A. C. Chibnall, *Proc. Roy. Soc.* (*London*) 131B, 136 (1942).
2. H. Jensen and E. A. Evans, *J. Biol. Chem.* 108, 1 (1935).
3. H. Gutfreund, *Biochem. J.* 42, 544 (1948).
4. E. J. Harfenist and L. C. Craig, *J. Am. Chem. Soc.* 74, 3087 (1952).
5. F. Sanger, *Biochem. J.* 39, 507 (1945).
6. A. H. Gordon, A. J. P. Martin, R. L. M. Synge, *ibid.* 37, 79 (1943).
7. F. Sanger, *ibid.* 44, 126 (1949).
8. ———, *ibid.* 45, 563 (1949).
9. R. Consden, A. H. Gordon, A. J. P. Martin, R. L. M. Synge, *ibid.* 41, 596 (1947).
10. F. Sanger and H. Tuppy, *ibid.* 49, 463 (1951).
11. ———, *ibid.* 49, 481 (1951).
12. F. Sanger and E. O. P. Thompson, *ibid.* 53, 353, 366 (1953).
13. ——— and R. Kitai, *ibid.* 59, 509 (1955).
14. A. P. Ryle and F. Sanger, *ibid.* 60, 535 (1955).
15. ———, L. F. Smith, R. Kitai, *ibid.* 60, 541 (1955).
16. H. Brown, F. Sanger, R. Kitai, *ibid.* 60, 556 (1955); J. I. H. Harris, F. Sanger, M. A. Naughton, *Arch. Biochem. Biophys.* 65, 427 (1956).

Elmer Martin Nelson, Government Scientist

Elmer Martin Nelson will be remembered for his important contributions to science, particularly in the field of nutrition. Evidence that eminence in the field of science can be attained in the service of government is clearly demonstrated in the career of this man, who was born in Clark, South Dakota, more than 66 years ago.

A man of stature, both physically and mentally, he possessed a delightful sense of humor, as well as the dignity and modesty befitting a "servant of the people." His firm but friendly attitude earned for him the respect and admiration of his associates. In the key position he held for many years in the Food and Drug Administration, his philosophy of law enforcement was to promote to the highest degree possible a voluntary compliance with pure food and drug law, through mutual understanding and respect. His straightforward discussion of difficult problems with scientists in industry led to increased confidence and developed a spirit of willingness to cooperate with the Food and Drug Administration. He continuously sponsored this theme of education and practiced frank discussion of enforcement problems with representatives of the food and pharmaceutical industries. In this association he helped to guide with integrity and knowledge the development and utilization of research in nutrition. The efforts of those who preyed upon consumers by exploiting new developments in nutrition science to their own commercial benefit were repugnant to his

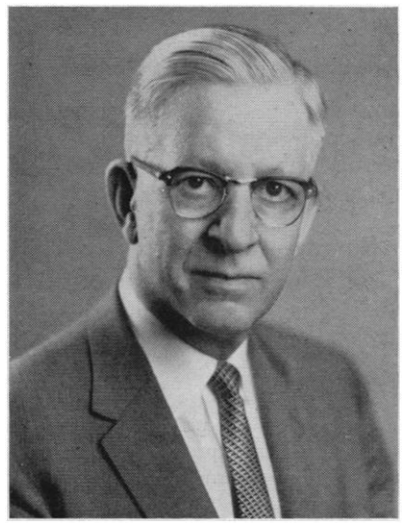
strong sense of scientific honesty. Through his lectures, his participation in symposia, his writings, and his testimony in many court contests, he was a leader in the campaign against quackery in the field of nutrition.

A dedicated scientist, he was actively interested in the training and development of the younger people with whom he associated. With his encouragement and guidance, a good number of his staff continued in graduate studies to complete their requirements for higher degrees. Those who had the privilege of working under his supervision will remember him as a stimulating and friendly teacher. Thorough and perceptive in his approach, he had a keen ability to detect the shortcomings of an experimental plan and to call attention to the over-all significance of experimental results.

His contributions to the scientific literature are many and varied. His service to the food industry was recognized in 1949, when he received the American Grocery Manufacturers' award. It was one of his proudest moments when, in 1957, the Babcock-Hart award was presented to him by the Institute of Food Technology.

A pioneer in vitamin research, he carried out his graduate and postgraduate studies at the University of Wisconsin under professors Steenbock and Hart during the period that saw the differentiation of vitamins A and D. His work contributed to knowledge of vitamin A—of its characteristics and the biological means for its estimation. His experiments pointed out the relationship between vitamin D and ultraviolet light and contributed to the basis for the Steenbook patent for irradiation of foods.

The year 1926 marked the beginning of what was to be a long and effective career in the broad field of public health. Early studies in the U.S. Department of Agriculture, conducted in association



Elmer Martin Nelson

with D. Breese Jones, provided important information in identifying selenium as the toxic agent in wheat grown in certain areas of the Midwest. During this same period much of his attention was devoted to the standardization of biological methods for measuring the fat-soluble vitamins—methods which later provided, in the *United States Pharmacopeia,* the first official tests for these substances.

When the time came in 1935 for the Food and Drug Administration to devote close attention to the many vitamin preparations appearing on the market, the logical choice for the leader of a group in this field was E. M. Nelson. Here it was felt his knowledge of vitamins and their place in nutrition could be utilized advantageously in the further development of methods of assay and related nutrition research. And so it was. Many of the studies conducted under his able tutelage resulted in the standard and official procedures now in use.

Elmer Nelson's name is recorded in scientific history as one of those responsible for the establishment of international standards for vitamins, an important step in the nutrition field. He was the United States representative to the first international conference on vitamins.

His associations in the American Medical Association's Council on Drugs and Council on Foods and Nutrition, his membership on the Vitamin Advisory Board of the United States Pharmacopeia, his activity on the Food and Nutrition Board of the National Research Council, his efforts as a general referee for the Association of Official Agricultural Chemists, and his extensive participation in many other scientific organizations provided close contact with eminent research workers and those influential in this field of endeavor. These contacts enabled him in his regulatory position to speak with authority on scientific matters and to disseminate his views most effectively as well as to have firsthand information of developments in the field of biochemistry and nutrition. He was thus well able to anticipate regulatory problems that might arise as a result of new findings on nutrition.

He was the principal nutritionist for the Government in the many public hearings that led to establishment of standards for enriched foods and of regulations pertaining to the labeling of foods that have special dietary uses. In his testimony he was ever mindful of the problems of the manufacturer, but he had as well an understanding of the phrase "to promote honesty and fair dealing in the interest of the consumer." He was a scientist to whom consumers the country over unknowingly owe a great debt.

His was a life of devotion to his profession. He was active to the very end, and his unexpected death, on 24 December 1958, came as a shock and brought great sorrow to his host of friends and associates.

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