SCIENCE

VOL. LXIX APRIL 12, 1929 No. 1789

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SCIENCE: A Weekly Journal devoted to the Advancement of Science, edited by J. McKeen Cattell and published every Friday by

THE SCIENCE PRESS

New York City: Grand Central Terminal.

Lancaster, Pa. Garrison, N. Y.

Annual Subscription, $6.00. Single Copies, 15 Cts.

SCIENCE is the official organ of the American Association for the Advancement of Science. Information regarding membership in the Association may be secured from the office of the permanent secretary, in the Smithsonian Institution Building, Washington, D. C.

THE WORK OF THOMAS BURR OSBORNE (1859–1929)

IT is given to few men to begin a scientific career with an investigation in an obscure and unattractive field, to continue their labors in it throughout a long and active life and ultimately to see this field become one of the most fertile and widely cultivated in their particular domain of science. The work of Thomas Burr Osborne on the vegetable proteins, continued from 1889 until his retirement in 1928, furnishes a striking example of a life devoted almost exclusively to scientific research upon a single group of substances and their derivatives. Owing to the diversified relationships of these substances this work has had a profound influence upon many phases of biochemistry.

Dr. Osborne was born in New Haven, Connecticut, on August 5, 1859. He was graduated from Yale University with the degree of B.A. in 1881, and received his doctorate from Yale in 1885. His dissertation was on "The Quantitative Determination of Niobium." From 1883 to 1886 he was an assistant in analytical chemistry at Yale and during this period published several papers dealing with analytical problems.

In May, 1886, at the invitation of Professor Samuel W. Johnson, professor of agricultural chemistry at Yale and director of the Connecticut Agricultural Experiment Station, Dr. Osborne became a member of the station scientific staff, forming a connection he retained until his death on January 29, 1929. Professor Johnson had become interested in Ritthausen's extensive studies of vegetable proteins. He was fully alive to their significance and suggested that further investigation was desirable. Accordingly, Dr. Osborne began in 1888 the labors that continued without interruption until his retirement.

Dr. Osborne's work on the vegetable proteins falls chronologically into three phases. From 1890 to 1901 the chief interest was in the preparation of pure specimens of the proteins of plant seeds. The initial investigation of the oat kernel, published in 1891, was followed by a series of papers in which the proteins from no less than thirty-two different seeds were described. Each of these was prepared, where possible, by a number of different methods; the criterion for purity and individuality was ultimate analysis for carbon, hydrogen, nitrogen and sulphur.

The properties of these substances were such as clearly to show the advantages for scientific investigation of the reserve proteins of seeds over the proteins of animal origin. Efforts to isolate proteins of definite properties from the complex mixtures in animal tissues had been for the most part unsuccessful, and even as late as 1911 ovalbumin was the only animal protein that had been clearly characterized as a chemical individual. On the other hand, many seed proteins were early shown by Dr. Osborne to be chemical individuals and preparations possessing identical properties were reproducible at any time.

A careful investigation was made of the proteins which had been previously grouped under the terms legumin, conglutin and vitellin, and it was shown that many of the proteins which thus had been brought together were, in fact, distinct substances. Specific designations were, therefore, in many cases coined and the use of the older names was restricted to those proteins to which they had first been applied. This clarification of the nomenclature has been of immense assistance in bringing a semblance of order into an almost hopelessly confused subject.

A few proteins had been previously prepared in crystallized form by other investigators. Dr. Osborne crystallized many of the seed globulins, and the readiness with which this could be done emphasized the fact that these proteins were definite substances entitled to the serious consideration of chemists.

The second phase of Dr. Osborne's work was initiated in 1899 with a paper[1] in which it was shown that the crystalline protein edestin from hemp seed forms two compounds with hydrochloric acid, a mono- and a di-hydrochloride, that the solubility of edestin in acid increases in direct ratio with the amount of acid present and that a number of crystallized vegetable globulins behave as bases neutralizing definite proportions of acid. In other words, the behavior of these proteins was that to be expected of basic substances of fixed composition. This was the end towards which his careful descriptive studies had been directed, a demonstration that proteins were definite chemical individuals. The position here taken was strengthened by later papers in which it was shown that proteins in general behave towards acid like bases, that they form salts both with acids and with alkalies and show many evidences of a capacity to undergo electrolytic dissociation and enter into ionic reactions.

These results emphasized the desirability of more complete chemical characterizations of the different proteins. The development of the methods of analysis of proteins at the hands of Hausmann, of Kossel and of Fischer furnished powerful means for supplying this and full advantage was taken of them. Furthermore, determinations of physical properties such as specific rotation, the heat of combustion and solubility in saline solutions contributed materially to the solution of the problem.

[1] T. B. Osborne, *J. Am. Chem. Soc.*, 1899, 21: 486.

By 1908, when the paper on "The Different Forms of Nitrogen in Proteins,"[2] perhaps Dr. Osborne's most widely quoted contribution, appeared, data had been accumulated which indicated clearly that few proteins had been obtained that could not be completely characterized by the methods of amino acid analysis, coupled with a study of the physical properties.

Beginning in 1906 and continuing for about six years, Dr. Osborne, with the aid of a number of collaborators, carried out a series of analyses of the amino acid composition of proteins by the Fischer ester distillation method. These studies set a standard for such work which has been surpassed only since the introduction in recent years of greatly improved methods for dealing with certain of the amino acids. Characteristically, he returned again and again to the analysis of a few of the proteins, such as casein, gliadin and zein, which possess special economic importance, each time increasing the summation of the components by the use of more refined technique. These analyses laid the foundation for the extensive studies of the nutritive properties of proteins that were begun in collaboration with Professor Lafayette B. Mendel, of Yale University, in 1909 and continued until 1928. This aspect of protein chemistry had attracted Dr. Osborne's interest from the earlier part of his career; but he had realized that until pure and uniform material could be obtained in abundance and its composition established by chemical analysis, an investigation of the comparative nutritive properties of proteins was useless. The striking differences which now became evident in the composition of many of the proteins suggested that their biological values might be correspondingly unlike.

It may be worth while to point out that in 1911 the notion that proteins might differ widely in nutritive value was relatively new. The chemical methods showed that wide differences in amino acid make-up occurred and, where these failed, the anaphylactogenic relationships, which had been studied in collaboration with Professor H. Gideon Wells, of Chicago, emphasized the difference in all save a few remarkable cases. But where wide chemical differences occurred, as between edestin and casein, both of which were found to be adequate for growth, it became necessary to suppose that the animal organism is capable of effecting

[2] T. B. Osborne, C. S. Leavenworth and C. A. Brautlecht, *Am. J. Physiol.*, 1908, 23: 180.

far more elaborate and extensive chemical transformations than had generally been thought.

The investigation of the nutritive properties of the proteins involved the development of a technique for feeding individual small animals which would permit accurate measurements of the food intake. This was successfully accomplished, but the first experiments in which the pure isolated proteins were fed, together with sugar, starch, lard and an inorganic salt mixture, showed that normal growth of young animals did not take place, although mature animals, as well as young, could be maintained for considerable periods. Growth of young animals could readily be secured when dried whole milk powder was furnished together with starch and lard. This appeared to indicate that milk contained something other than protein essential for growth. The preliminary assumption was made that the missing factor might be supplied by the inorganic constituents of the milk, and it was found that excellent growth could be secured when evaporated milk serum from which casein and lactalbumin had been removed, the so-called "protein-free milk," was added in sufficient amounts to a diet of isolated protein, starch and lard. With the assistance of this material an extensive investigation revealed wide differences in the alimentation of animals on different proteins. Animals rapidly failed on zein and gelatin, were maintained on hordein, rye and wheat gliadin, but grew well on edestin, wheat glutenin, lactalbumin or casein. Further work showed that the failure of animals on a zein diet was due to the lack of tryptophane and lysine in this protein. When these amino acids were supplied growth occurred. Similarly, gliadin could be made adequate for growth by an addition of lysine in which this protein was conspicuously deficient.

The use of protein-free milk in diets was attended by certain difficulties. It was not entirely free from nitrogen and it could not be successfully replaced by an artificial mixture of salts made to imitate the composition of milk ash as closely as possible. Furthermore, animals nourished on this diet over long periods ultimately ceased to grow and declined rapidly in weight. In every case such animals could be brought to a normal rate of growth by changing to a diet containing whole milk powder, and the ultimate failure on protein-free milk could be postponed or averted by feeding whole milk powder for occasional short intervals. An examination of the composition of the two types of food revealed that the most conspicuous difference lay in the presence of milk fat in the dried milk food. Experiment soon showed that the addition of butter to a casein, starch and protein-free milk diet sufficed to permit normal growth to maturity. When butter was added to a diet of dried skim milk upon which it had been found that animals ultimately failed, complete realimentation occurred.

These results were published in 1913. The paper describing them was submitted to the *Journal of Biological Chemistry* about three weeks after a paper by McCollum and Davis in which similar results, secured by the use of an ether extract of egg yolk and of butter, were described. The observations indicated that a substance occurs in butter which is essential for animal growth. This substance was later designated as vitamin A.

In the following year the important observation was made that the same stimulation of growth could be secured by the addition of cod-liver oil to a diet of purified food substances and protein-free milk, a discovery which served to focus attention upon the value of this oil, in particular as a curative agent for the peculiar eye condition known as xerophthalmia that was regularly encountered by Osborne and Mendel in animals on the deficient diets. At the close of the war the sight of many children in Europe was preserved by its use, a remarkable example of the application of scientific results to practical problems.

The later extensive contributions of Dr. Osborne and his associates to the science of nutrition can only be indicated. Much labor was devoted to the study of the nutritive value of the proteins of the commercially important foods and this work gave a rational explanation of many practices which empirical experience had shown to be advantageous. The distribution of vitamins A and B in natural food products was studied and considerable success was attained in an effort to prepare a vitamin rich concentrate from yeast. The phenomena of growth, its suppression and acceleration under various regimens, the effect of the individual inorganic constituents of the diet, these and many other topics received attention at different times.

The remarkable influence of minute traces of certain organic substances, the presence or absence of which in the diet determine success or failure of nutrition, drew attention to the importance of an investigation of the constituents of living cells. This led to a detailed study of extracts of the alfalfa plant and of yeast, both of which are valuable sources of vitamins. Much of the information secured did not reach the stage of publication, but a striking demonstration was obtained of the complexity of the chemical environment in which the life process takes place.

It would be incorrect to assume that Dr. Osborne's interest in the fundamental chemistry of proteins waned as he penetrated more deeply into the mysteries of animal nutrition. Innumerable chemical problems arose as a result of the feeding work and demanded solution. Such, for example, was the discovery in 1913 of lysine among the products of hydrolysis of gliadin: its presence had escaped the notice of previous observers, including himself. A study of the constituents of milk in 1917 revealed a new protein soluble in diluted alcohol, the first animal protein possessing this property to be found. Its anaphylactogenic relationships were worked out in collaboration with Professor Wells in 1921, and it was demonstrated to be distinct from the other three proteins of milk.

Dr. Osborne made a fundamental contribution to the chemistry of nucleic acids in 1900, when he announced the discovery of tritico-nucleic acid in the wheat embryo and observed that this substance yielded the purines, guanine and adenine, in molecular proportions. Subsequently he made it clear that the various nucleoproteins which could be prepared from the wheat embryo were in reality salt-like compounds of one and the same protein with variable proportions of nucleic acid. Generalizing from these observations he pointed out that the numerous nucleoproteins from animal sources that had been described were, very probably, also salt-like compounds of protein with nucleic acid.

Although all the preparation work and much of the chemical investigation of the proteins was done before the modern conceptions of acidity had been advanced, Dr. Osborne was aware of the influence of different degrees of acidity on his preparations. One of his early papers on the effect of small amounts of acid on edestin[3] contains the phrase "the concentration of the hydrogen ions in the solution," and it was his custom invariably to state the indicator which he used. It was not sufficient to neutralize a solution; the solution was neutralized to phenolphthalein, or litmus, or tropeolin, as the case might be, and the differences in behavior so indicated were fully appreciated. It is this meticulous attention to detail which gives Dr. Osborne's early work a value to the present-day physical chemist and renders it possible to furnish an interpretation in terms of modern theory, as has recently been done by Cohn.

Dr. Osborne was one of the most distinguished pupils of Professor S. W. Johnson, and through him traced his intellectual ancestry back to Liebig, the founder of agricultural chemistry. A painstaking, careful investigator who spared no effort, time or expense in the attainment of the truth, Dr. Osborne accepted no result until it had been subjected to the test of rigorous and repeated experiment and all his publications bear the marks of meticulous editing, lest a statement should to the slightest extent pass the bounds of ascertained fact.

[3]T. B. Osborne, *Ztschr. f. Physiol. Chem.*, 1901, 33: 225.

To those who were privileged to be associated with him in his work he was a rare stimulus, a formidable opponent in argument and an ever genial but just critic. He frequently closed a discussion with the remark that facts were to be found in the laboratory, not in the books. Naturally shy and retiring, the delivery of a public address or of a paper was a severe trial to which he looked forward with trepidation. But among a small group of friends he showed himself as a gifted conversationalist, who was equally able to discuss the latest achievements of science, the current political situation, the intricacies of the world of finance or the faults of the modern educational system.

The first public recognition of Dr. Osborne's exhaustive work came from Germany. V. Griessmayer, in 1897, published a book on vegetable proteins that contained many extracts from Dr. Osborne's papers and stated in the introduction that it was his object "to bring to light these treasures buried in their American publications." This encouragement, at a time when few of his associates or scientific friends had any conception of what his work meant, was of great assistance to him.

In 1900 he was awarded a gold medal by the Paris Exposition. In 1910 recognition came from Yale University in the form of the honorary degree of Sc.D., and in the same year he was elected a member of the National Academy of Sciences. Two years later he was made an honorary fellow of the London Chemical Society, and in 1914 he was made a fellow of the American Academy of Arts and Sciences.

In 1922 he received the John Scott medal and in the following year was made a research associate in biochemistry of Yale University with professorial rank. In 1928 he was the first to receive the Thomas Burr Osborne gold medal founded by the American Association of Cereal Chemists in recognition of his outstanding contributions to cereal chemistry.

Dr. Osborne's extensive investigations would have been impossible without generous financial support and encouragement. Throughout the early years, when results came slowly and their application was by no means apparent, the directors of the Connecticut Agricultural Experiment Station, in the early years Professor S. W. Johnson, and after 1900, Dr. E. H. Jenkins, with the cooperation of an enlightened board of control, allowed no interference or distraction to hinder the progress of the work. Since 1904 a large proportion of the financial burden has been borne by the Carnegie Institution of Washington, D. C., of which he was a research associate. Dr. Osborne's connections with both the experiment station and the Carnegie Institution of Washington furnish a striking example of the value to science of a policy of non-interference on the part of those in control of the distribution of funds for research. Except for routine annual reports he was never asked for statements of progress or for outlines of projects. The relationship was always one of the utmost mutual confidence and esteem.

The results of Dr. Osborne's investigations were summarized in a monograph, "The Vegetable Proteins," which first appeared in 1909 and was extensively revised in 1924. This slim volume has become the classical publication in the field. His extensive studies of wheat proteins were reviewed in "The Proteins of the Wheat Kernel" (1907), now a standard text among cereal chemists. Including these and a few public addresses and popular articles a complete bibliography of his publications reaches 253 titles, of which about two hundred are journal reports of his personal scientific work.

Dr. Osborne's most marked characteristic was, perhaps, the thoroughness with which his problems were investigated. In the early preparation work each protein was isolated in as many different ways as possible, the composition finally ascribed to it was deduced from a large number of carefully conducted analyses and, where the economic importance of the protein warranted it, he returned again and again to its study. The wheat and maize prolamins received extraordinary attention and the methods of preparing even these well-known substances were recently, with the aid of his assistants, materially improved. Time and again he discarded the whole of his painfully acquired results to make a fresh start, this time to "do it right," as he expressed it. His death removes one of the great pioneers of American biochemistry, a man whose name will always be linked with the subject he made peculiarly his own. He was more fortunate than most men in that advancing years, distinctions and scientific recognition did not bring with them administrative responsibilities that deprived him of the opportunity to share in the daily work of the laboratory. His time was always freely available for discussion, not only with his associates, but with the innumerable investigators from all parts of the world who came to New Haven to see him and ask for advice. Ever kindly and courteous, with keen insight into the problems of others and an extraordinary wealth of experience upon which to form his judgments, he has left a memory that will long be treasured by those who had the privilege of knowing him.

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Connecticut Agricultural Experiment Station

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Yale University

THE OBJECTIVES OF UNDERGRADUATE COURSES IN PHYSICS FOR ENGINEERING STUDENTS[1]

Freeing myself, for a moment, from the restrictions implied by the above title, I wish to make some general observations concerning what seem to me to be the two superlatively remarkable aspects of present-day physical science.

(A) The first aspect relates to *the ability of the trained physicist to hold things in mind.* The clear and sharp concepts of the kinetic theory of gases, for example, constitute an actual working model of a gas, a working model which exists in one's head! And every physicist knows how this model helps one to hold gas-facts in mind and how tremendously it helps one to think about gas-facts.

Helmholtz, in commenting on the postulated or assumed elements which enter so largely into our conceptions of physical conditions and things, goes on to say "it is nevertheless a great help if we form in every case the most concrete possible picture, even when the picture contains many an assumption that is not, in all strictness, necessary."

(B) The second aspect relates to *the extent to which quantitative mathematics can be tied to physical conditions and things.* Every quantitative notion in physics *is* or *grows out of* a precise idea. Thus velocity is a precise idea; acceleration is a precise idea; electric current strength is a precise idea. In tying mathematics to physics nothing else is so essential as precise ideas, and it is an extremely remarkable fact that "the possession of precise ideas opens the mind," as Whewell has said, "to an almost endless array of simple perceptions which would be, without the use of precise ideas, non-existent."

Regarding these two things (A) and (B), I believe the time will come when every man who has to deal with physical things will have to be equipped with all of the more important concepts and with all of the more important precise ideas of physics, and trained to use these concepts and ideas effectively.

However remote the realization of this ideal for all working men may be, it is certainly now the main objective of the teaching of physics in the college and the engineering school; and, although the teacher of physics in the college can, perhaps, neglect this objective to some extent, the teacher of physics in the engineering school can not neglect it at all, and it is an objective which holds in the preparation of young men for research, even more rigorously, than in the preparation of young men for practical work.

[1] A paper read before the Summer Conference of Teachers of Physics to Engineering Students, Massachusetts Institute of Technology, July 13, 1928.