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FACULTY RESEARCH LECTURE
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THIRD ANNUAL FACULTY RESEARCH LECTURE

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THE FACULTY ASSOCIATION

UTAH STATE AGRICULTURAL COLLEGE

LOGAN, UTAH, 1944

THIRD ANNUAL FACULTY RESEARCH
LECTURE DELIVERED AT THE COLLEGE
APRIL 27, 1944

THE following lecture by Mrs. Almeda P. Brown is the third in a series to be presented annually by a scholar chosen from the resident faculty at the Utah State Agricultural College. The occasion expressed one of the broad purposes of the college Faculty Association, which is a voluntary association of members of the faculty. The 1944 lecture appears under the Association's auspices as defined in Article II of its Constitution, amended in May 1941:

> The purpose of the Organization shall be . . . to encourage intellectual growth and development of its members . . . by sponsoring an Annual Faculty Research Lecture . . . The lecturer shall be a resident member of the faculty selected by a special committee which is appointed each year for this purpose and which shall take into account in making its selection, the research record of the group and the dignity of the occasion . . . The lecture shall be a report of the lecturer's own findings in a field of knowledge . . . The Association shall express its interest by printing and distributing copies of the Annual Faculty Research Lecture.

Mrs. Brown was elected by the committee to the third lectureship thus sponsored. On behalf of the members of the Association we are happy to present Mrs. Brown's paper: "NUTRITIONAL STATUS OF SOME UTAH POPULATION GROUPS."

COMMITTEE ON FACULTY RESEARCH

FOREWORD

THE science of nutrition is the science of life. Though man is still ignorant of the true nature of that elusive force we call life, he has learned by means of the discovered laws of nutrition how to preserve and prolong life as well as how to add to the satisfactions of living.

The emergence of the sicence of nutrition from the maze of superstition which for centuries clouded man's thinking is a fascinating story. A story, however, that arouses a feeling of regret that for so long a time man was willing to attribute to supernatural forces all phenomena that were to him not easily explainable.

This tendency to superstition together with the effortless efficiency with which the healthy body functions, obscured for a long time the relationship between ingested food and bodily development and activity. Small wonder, therefore, that Galen and Paracelsus, dimly aware of the body's smooth functioning, were willing to credit their so-called "natural spirits," or "vital spirits," with the operation of a splendid mechanism that was beyond their understanding.

To Vesalius is due in large part, the beginning of a substitution of observation and inquiry for unthinking superstition. The science of nutrition as we know it today is greatly indebted to the fact that Vesalius was able to impress his many capable and influential students with the value of this substitution.

Almeda Perry Brown
Logan, Utah
April 27, 1944

ACKNOWLEDGEMENTS

MANY persons have contributed to the conduct of these studies, for whose contributions grateful acknowledgements are herewith offered.

First of all to the Utah State Agricultural College administration, specifically to the several directors of the Experiment Station, who provided the means for accomplishing the work of the various projects; to the group of farm families who kept faithful dietary records over a long year; to school children, their parents, and to school officials, without whose cooperation dietary surveys would have been impossible; to physicians and dentists who contributed their valuable professional services without remuneration other than the satisfaction of a good piece of work well done. Particularly is the deepest gratitude due the College Physician, Dr. W. B. Preston, for continued assistance and support over the period of these studies.

Grateful acknowledgement is offered the many college students who took time out of a busy day to serve as subjects, often for several different types of tests including long, tedious anthropometric measurements. Much credit also is due the several students, among them Lydia Jennings, Beth Merrill, and Vera Greaves, who aided in the collection of data and their analysis. Tribute is paid the friend and assistant, Faye Moser, who over a period of years gave loyal support and assistance. Acknowledgement is made with keen appreciation of the encouragement and aid of the Northwest Cooperative Nutrition Research group.

Last, but by no means least, the privilege provided by the Committee on Faculty Research for reviewing in brief form this series of studies is acknowledged with gratitude. It is sincerely hoped that the pointing out of certain dietary deficiencies found among large numbers of Utah residents will result in earnest efforts to eradicate such deficiencies.

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SIGNFICANCE OF NUTRITION

NUTRITION has come to be a word of greatest significance. Significant because scientists, diplomats, officials, and laymen have recognized the importance of nutrition to the man at the front fighting to preserve a democratic way of life, to the producer of materials, and to the civilian backers of these groups; probably most of all to the boys and girls whose task it will be to build a new world after the victory is won.

One indication of the universal recognition of the importance of nutrition is seen in the United Nations Conference on Food and Agriculture held at Hot Springs, Virginia, May 18 to June 3 of last year (1943) with representatives of 44 countries in attendance.

Whether this conference will stand out as a magnificent war-time gesture, or will mark the beginning of an international program of adequate nutrition for the peoples of the world, will depend upon how seriously the permanent organization provided for by the conference considers its assignments. Only the years following the victory will tell.

Nutrition as a science is one of the youngest in the family of sciences. An outgrowth of chemistry and of physiology it had its foundations in the work of a French chemist, Antoine Laurent Lavoisier, in the latter half of the 18th century. In the century and a half since the death of Lavoisier, the science has grown to proportions such that only specific phases can be treated in a paper having the proportions of the present one. After short pauses, therefore, at some of the milestones along the way and with brief reference to some pertinent research procedures, this discussion will concern itself with the investigations at this institution into the nutritional status of some population groups within the region served by the Utah Agricultural Experiment Station.

EARLY CONCEPTIONS OF NUTRITION

IT is probable that one of the earliest observations on nutrition was that adults, though ingesting considerable quantities of food year after year, changed their size little or not at all. Hippocrates, philosopher and Father of Medicine, who lived from 450 to 357 B.C, explained this phenomenon on the basis of loss by "insensible perspiration" and by the elimination of heat, which, he believed, was a refined form of matter. He had an interesting theory to the effect that no matter what the variety of foods eaten there was extracted from them but one "aliment" or nutritional factor. By later nutritionists he is credited with the paradoxical statement, "There are many aliments, but only one aliment."

This idea of a single nutritive factor seems to have prevailed unchanged through many centuries, during which time little progress was made in any of the areas of human knowledge. One of the earliest in the awakening after the Dark Ages to enunciate theories on nutrition was Paracelsus, a Swiss physician and chief among iatrochemists (1493-1541). He explained the mysteries of nutrition by assuming an "Archeus" or vital spirit, resident in the stomach, that directed the continuation of life by separating food substance into their good and bad elements, discarding the latter, and providing the former for use of the various organs of the body.

Between the passing of Paracelsus and the coming of Lavoisier a series of chemists, most of them of the iatro or medico type, contributed bits of information which, as they gradually came to be pieced together, gave direction to man's thinking on the nature of the vital processes.

THE FOUNDING OF A SCIENCE

THE many accomplishments of Lavoisier (1743-1794) during his brief 51 years of life entitle him to recognition as one of the most versatile and brilliant men of all times. Designated by his countrymen as the Father of Chemistry and recognized by nutritionists as the founder of the science of nutrition, he was also an economist, a financier, and a scientific farmer.

Though previous investigators had questioned the phlogiston theory of combustion, and Boyle, Scheele, and Priestly had noted the involvement of an atmospheric gas in the process, Lavoisier was the first to recognize the true nature of combustion and to give the name "oxygen" to the gas involved. He declared that the life processes are those of slow oxidation with elimination of heat. He contrived devices for measuring heat given off by the animal body and discovered some of the factors which affect amount of heat eliminated, such as surrounding temperature, kind and amount of clothing, and exercise. He thus laid the foundation for and gave direction to future study of energy metabolism.

His continued combustion studies together with other chemical investigations led to the information that organic substances contain carbon and hydogen and sometimes oxygen, with nitrogen occurring less often and sulfur and phosphorus sometimes. He is credited therefore with initiating organic analysis.

After Lavoisier, chemists and physiologists followed the two lines of investigation started by him. While one series investigated the composition of foods and learned something of their behavior in the body, another series continued the investigation of energy metabolism.

Francois Magendie (1783-1855), French physiologist and important link between the work of Lavoisier and Liebig, was one of the first to discredit in a serious way the one-aliment theory, and in doing so to set the pattern for modern nutritional research by the biological method, and to lay the foundation for modern theories of metabolism.

Boyle had used frogs, kittens, and ducklings in respiration studies, Lavoisier had used guinea pigs in determining body heat, but Magendie pioneered in the use of animals for study of nutritive values of foods. In this way he showed conclusively that various food substances are decidely different in their ability to sustain life and promote growth of animals. He distinguished clearly between nitrogenous and non-nitrogenous foods and showed that nitrogen in animal tissues is there as a result of ingestion of nitrogen-containing substances and is not converted within the organism from a universal aliment.

G. J. Mulder (1802-1880), a Dutch physiological chemist, recognized nitrogenous substances in plants similar to those in the animal organism. He wrote, "In both plants and animals a substance is contained, which is produced within the former, and is imparted through their food to the latter. To both, its uses are numberless. Through its means the chief phenomena of life are produced" (17). In 1839 Mulder gave the name "protein" to this very important substance.

Justis Von Liebig (1803-1873), one of the most outstanding chemists and teachers of chemistry of the 19th century, developed the pattern of modern organic analysis begun by Lavoisier. He began also the accumulation of knowledge on the chemical composition of foods and of body excretions. He conceived the idea that nitrogenous foods serve for building body tissue and as a source of energy for muscular work, believing that destruction of muscle tissue was in proportion to work performed. This theory was later shown by Voit to be erroneous. He advanced the theory that nitrogen appearing in the urine may be considered a measure of protein metabolism. Liebig's researches in organic substances directed some of his energies into the field of agricultural chemistry, and he was influential in converting the German government to the provision of funds for establishment of agricultural experiment stations. The first one was established at Möckern, near Leipzig, 1851-52. Twenty-five years later there were 74 such stations in Germany. At each station a chemist with one or more assistants was engaged in the analysis of foods, feedstuffs, fertilizers and other agricultural products, and in conducting experiments on the fertilization of crops, and the feeding of farm animals.

Among Liebig's pupils were a number of Americans who became leaders in the development of agricultural and related chemical research in the United States. An outstanding member of this group was Samuel W. Johnson (1830-1909), who on his return to America became professor of analytical chemistry at the Sheffield Scientific School at Yale; he became also chemist for the Connecticut Agricultural Society. It was largely through Johnson's influence that Connecticut established in 1875 the first state experiment station, with W. O. Atwater as director. Both Johnson and Atwater were influential in obtaining passage of the federal act in 1887 which provided for an experiment station in each of the United States. The work of these stations followed the general pattern of the European stations.

Following the respiration and energy studies of Lavoisier, Dulong and Depretz improved upon his guinea-pig-in-a-block-of-ice equipment by placing a laboratory animal in a double chamber with water in the outer one to absorb heat eliminiated from the animal body.

Later Regnault and Reiset constructed a closed circuit respiratory apparatus employing the same principle used in modern closed circuit apparatus. With it they studied the respiratory quotient and the manner in which different food types affect it.

Voit, professor of physiology at Munich, and Pettenkofer, director of the Munich hygienic laboratory, constructed respiration apparatus by means of which they determined, during the same period, total carbon elimination through respiration, and total nitrogen elimination through urine and feces. Rubner, a pupil of Voit, constructed a calorimeter and attached it to the respiratory apparatus of Voit and Pettenkofer.

Atwater, an American pupil of Voit, constructed, with the aid of the physicist, Rosa, a respiration calorimeter large enough to carry on experiments with human subjects.

It was now possible to see in its broad outlines a picture of human metabolism and to make fairly reliable estimates of human needs for various food factors under differing conditions of age, size and activity.

Combining this information with his observations of the dietary habits of Munich citizens, Voit constructed tables of dietary standards specifying amounts of fats, carbohydrates, and proteins, required by people of both sexes at hard work, moderate, and light work, and at different age levels. Similar standards were subsequently set up in England by Playfiar, in France by Gautier, in Amercia by Atwater, Chittenden, and Langworthy. Continued research since the setting up of these standards has established information concerning quantitative human requirements for various minerals and vitamins as the need for these foods became known. The most recent standards generally accepted by nutritionists are those tentatively set up by the Food and Nutrition Committee of the National Research Council, commonly referred to as the "nutrition yardstick."

The accumulation of information on nutritive values of foods which began with Lavoisier, had now reached a stage where it was possible to tabulate in classified form the chemical composition of an extensive list of human foods. In Germany this was first done by Voit, in England by Hopkins, and in America by Atwater. In the words of McCollum (14), "This marked one of the great epochs in the development of the science of nutrition." The setting up of dietary standards and of lists of food values was followed by a large number of statistical dietary studies centering in experiment stations and published in bulletin form by the stations or by the United States Department of Agriculture.

The general plan of these studies consisted of (a) collection of data on kinds and amounts of food eaten by the group under investigation over a period of time agreed upon; (b) computation of nutritive value of dietary by aid of tables of food values; (c) evaluation of adequacy of the diet by comparison with an accepted standard of good nutrition.

Notwithstanding criticism of this method because of possible errors in collection and interpretation of data, it is still useful in making dietary survey of groups, and was recently defended by Nutrition Review (1:72, 1943) on the grounds that it furnishes the best means now available for uncovering likely areas of malnutrition before severe degrees of deficiency develop. Recent government reports on the prevalence of subnutrition in the United States are based in large part upon this type of study.

NUTRITION STUDIES AT UTAH AGRICULTURAL EXPERIMENT STATION

Dietary Surveys Revealing Certain Deficiencies. The first investigation of nutritional status at this institution was of the statistical type and the population group concerned was the farm famliy. The only thing unique about it was that the period of time covered was one year. The forty-three housewives who weighed and recorded all foods served to their families for so long a period accomplished a feat, which, so far as my knowledge extends, has not been equalled at any time, anywhere.

Analysis of the data on their records showed their year's dietaries to be adequate in caloric value for a group such as theirs at moderately hard work, however, they were inadequate in content of iron, phosphorus, and animal protein. If farm families are to be considered as a hard working class the dietaries were inadequate in caloric value also. Deficiencies were caused by insufficient use of lean meat and of fruits and vegetables, all of which should be available to farm families in quantities needed by them. Recent studies reviewed by the National Research Council show these same deficiencies in farm family diet over wide areas in the United States.

The second population group studied consisted of 891 children between the ages of 6 and 14 years in three different counties. The approach was through the public schools where dietary information was obtained from two-day menus supplied by the students each month during a school year. The average score of these 891 dietaries on the basis of 100 points was only 54. The reason for this low average was that scores for all types of foods were from one-half to two-thirds of maximum. As in the study of farm family diet the foods most neglected were lean meat, fruits and vegetables. Green vegetables very rarely appeared in the menus.

Attemps were made to correlate low dietary scores with various physical defects found by physicians and dentists in a special examination of each child. A low order correlation between the number of cavities in permanent teeth and quantity of milk ingested daily was the only specific relationship found between diet and physical status. However, the study did stimulate the thinking of both children and parents upon nutrition and health as related concepts.

Biological Study Revealing Vitamin Deficiencies. At the time these studies were made vitamins were less well known than at present, but their importance in nutrition was generally recognized. Because of restricted use of vegetables among groups surveyed the question of possible vitamin deficiencies obtruded itself. The biological method was then the only approved procedure for detecting vitamin deficiencies. Arrangements were made, therefore, for testing on laboratory animals, a diet of the same design as that of the 891 children. Guinea pigs fed the diet without addition of vitamin C developed scurvy within three weeks; some of them died, and at autopsy showed charateristic lesions of scurvy. Those which survived to the end of the experiment showed at autopsy scurvy scores of 10-17 out of a possible score of 24. Guinea pigs given a vitamin C supplement of orange juice or tomato juice, survived without displaying any symptoms of scurvy and showed at autopsy a zero scurvy score.

Other vitamins recognized at that time were A, D, B_1, B_2, or G. Albino rats were used in the study of these vitamins.

Animals on the diet of the school child without additions made slow steady growth but remained relatively small even after reaching adulthood. With each addition of a vitamin to the diet the animals showed better growth, the best growth was attained by those having all four vitamins under investigation.

The evidence appears to point to the inadequacy of the diet reported by these children to protect guinea pigs from scurvy and otherwise to support maximal growth and well-being of laboratory animals. The slow growth and small size of rats on the unsupplemented diet may have significance in the fact that height-weight-age measurements of these 891 children in rural schools showed them to be. in the main, below average size when compared with the Baldwin-Wood height-weight-age tables. A larger sample including 12,913 children from rural schools in twenty-one Utah counties showed the same size pattern; height-weight-age measurements of 13,831 children in city schools of the state showed them to be generally about one inch taller, and from 1 to 5.5 pounds heavier than rural children of the same age. Still these city children were not above average size when compared with Baldwin-Wood tables.

The possibility of these differences being a result of better nutrition of city children was investigated. Nutritional status indices reflecting amounts of musculature, subcutaneous tissue, and weight, in relation to skeletal structures were computed for representative samples of both rural and city children by the method of the Child Health Association[1] and were submitted to analysis of variance. The only significant differences (F values above the 5 percent level) found on the basis of rural and city residence were those for weight indices and there the probability was only 19 to 1. It appeared, therefore, that recent nutrition did not cause the differences in size, since the relationship of soft tissues to skeletal structure was practically as good for the smaller rural children as for the larger city children. In this

[1]The American Child Health Association. Nutritional status indices. Method of obtaining measures of musculature, subcutaneous tissue, and weight, with allowance for skeletal build. New York, 1935.

connection the parallelism between the relatively small size of this large number of children and the small size of rats fed on the school child's diet is too significant to be overlooked.

The Capillary Resistance Test. About the time these studies on school populations were in progress Gutaf F. Göthlin (8), a Swedish physiologist, published his capillary resistance test for determining human requirements for vitamin C. This marked the beginning of quantative vitamin C studies with human subjects. Practical methods for study of other vitamins came later.

Reasoning from the fact that in manifest scurvy, blood vessels become so reduced in strength as to rupture voluntarily under the strain of normal blood pressure, Göthlin postulated that lesser degrees of vitamin C deficiency might be made to manifest themselves in the same way if external pressure were applied.

Beginning with the blood pressure tourniquet used by clinicians, Göthlin developed additional equipment and perfected techniques for detecting vitamin C subnutrition. The degree of subnutrition was measured by the number of petechial hemorrhages appearing in a 60-mm circle marked off in the antecubital fossa in response to pressure applied for a period of 15 minutes through the blood pressure tourniquet.

A simple variation of the capillary resistance test, sponsored in this country by Dalldorf (6), of the Grasslands Hospital, New York, consisted of applying a 2-mm vacuum cup, connected with a vacuum pump and a manometer, to the outer surface of the upper arm for one minute. The vitamin C standard was determined by the amount of negative pressure or suction required to produce macroscopic petechiae in the area covered by the vacuum cup.

These tests appeared to offer a means of determining directly the extent and degree of vitamin C deficiency which, as indicated by guinea pig reaction, probably existed among rural Utah children. Permission was obtained from parents and school officials to apply the tests to 215 children in grade schools of Cache County and to 81 high school pupils in the southern part of the state. Tests were also given to 336 college students. The Göthlin technique was used except with small children who were unable to sit still the required 15 minutes, with these the Dalldorf technique was used.

Göthlin (8) emphasized the importance of information on dietary habits of subjects in interpreting results of the tests. Investigators, therefore, learned through conferences with children and parents the kinds of fruits and vegetables eaten at the time of the test and the number of times each appeared on the menu daily, also the number of apples, tomatoes, or other such foods eaten between meals.

Of the 215 children tested in the fall by the Göthlin technique only one child responded with a large number of petechiae; 12.5 percent reacted with numbers of petechial hemorrhages that placed them at the positive or borderline level, which means an average of less than 8. By Göthlin's scale, as finally developed, an average of 0-4 petechaie following a double-arm test at 50-mm pressure, indicated normal standard; 5-8 borderline, and above 8 a positive deficiency. At the spring examination the number of borderline and positive reactors had risen to 20 percent, and the average number of petechiae per child had increased from 3.6 to 5. Tests by the Dalldorf technique showed in the spring an average reduction of from 3 to 5 cm. in amount of pressure required to produce macroscopic petechial hemorrhages. The number of times vitamin-C-containing foods appeared in the diet had decreased from 5 to 2. In addition such foods eaten in the spring consisted mainly of canned or stored fruits and vegetables, hence were probably less efficient as sources of vitamin C.

These data indicate that one-eighth of a fairly large number of children were in a mild state of vitamin C subnutrition when tested in the fall, and that during the winter the proportion increased to one-fifth of the group accompanied by corresponding decrease in vitamin C value of foods ingested.

The 81 high school students showed a higher percentage of positive and borderline reactions at the fall test (21 percent), but the increase at the spring test was only 2 percent, and there was an average increase of only 1 petechia per person.

The results of tests on college students were less clear cut, possibly because of greater refinement of procedure. Participating college students had as an assignment for a course in nutrition, the keeping of a week's food record; foods were reported quantitatively either by weight or measure. The computed average number of units of vitamin C in the week's dietary and the number of petechiae resulting from the capillary resistance test were plotted against each other on a scatter diagram; no significant correlation was indicated. The reason for this lack of correlation, investigators believed, was owing either to inaccuracy of dietary records or to insensitivity of the test.

Turpeinen (23) discussed a study in which computed ascorbic acid intake of 616 persons was correlated with the number of petechiae resulting from the capillary resistance test. Though the coefficient of correlation was of practically the same order as that found in our study, he concluded that a correlation existed between the ascorbic acid content of the diet and capillary fragility, and suggested various factors, among them possible inaccuracies in dietary data, that may have been responsible for the low correlation coefficient. Investigators, both in the United States and elsewhere, failed to get the clear-cut indications of vitamin C deficiency with the capillary resistance test that were reported by the Swedish group, hence the test did not receive wide popularity.

Answering criticisms of his test on the basis of the inability of American and other workers to obtain results comparable to his own, Göthlin emphasized the fact that it had been developed for people of the Nordic race only. In an investigation of vitamin C standard made by Göthlin and associates in the north of Sweden where some race mixture of Nordic with East Baltic and Lapp existed, "certain race-biological observations" were made in connection with the capillary resistance tests. This they did "with the object of validating the results if in the future it should be found that in the Lapp race or in an individual with mixed blood, the degree of capillary strength is not the same as that of a person of the Nordic race" (7). To investigate the probability of race as a factor in determining our results, information was obtained on nationality of parents and grandparents of all college students tested. In addition a series of anthropometric measurements were made and intricate indices were computed; color of hair and color of iris were determined according to color scales in use at the State Institute for Race Biology.

Information on nationality showed the parents and grandparents of subjects to be predominantly American with a few English, German, Swiss, and Scandinavian. Among those of mixed nationality English with American predominated. Differences in reaction to the test could not be detected on the basis of nationality. Subjects of German and of Northern European ancestry with the blond hair and blue eyes, assumed to be characteristic of the Nordic race, did not show more marked reaction than did those of darker complexion. Subjects with thin skin of fine texture reacted more readily than did others, and this type of skin was encountered as frequently among third generation American and those of English parentage as among subjects of German and Northern European ancestry. Cephalic index for all national groups varied little from the average value of 79. Indices computed from other head and face measurements as well as computed indices of size and body build did not vary greatly among the subjects, and none of them appeared to be related to degree of reaction to the capillary resistance test.

We were led to question the pressure used in our tests by the Göthlin technique because of the relatively few cases encountered that reacted with a large number of petechiae. Göthlin originally used three pressures, 35, 50, and 65 mm. Hg.; later he discarded the 65 mm. pressure. By means of repeated tests made over a period of three months on a group of 27 young women living in a dormitory, whose diet was computed to be adequate with respect to vitamin C, it was found that the pressure required to produce petechiae between 0 and 4 (which Göthlin considered the normal range) was 48 mm. This gave assurance that the 50 mm. pressure could be considered standard for our subjects.

By similar procedure we learned that normal, healthy young men and women tested by the Dalldorf technique would withstand a negative pressure of 20 cm. without macroscopic petechiae. This was a lower pressure than that reported by Dalldorf (6), but was in agreement with reports of Jersild (13).

After the blood plasma method was established, Göthlin (9) reported studies to show that the capillary resistance test revealed only such degrees of vitamin C deficiency as were marked by blood plasma concentrations of 0.1 to 0.14 mg/100 ml. which is much below the generally accepted minimum of 0.6 mg., considered to be the lowest level of normal vitamin C nutrition. In view of these findings Göthlin suggested that in countries where vitamin C foods are plentiful as in the United States, it is quite possible that deficiencies of the vitamin severe enough to be detected by his capillary resistance test are less common than in his native Sweden. There the season for growing fruits and vegetables is relatively short and variety and quantity of vitamin C foods limited.

More than 300 subjects have been tested by the blood plasma procedure at this institution and but one man and one woman have been found with levels as low as 0.16 mg. per 100 ml. The test appears therefore not sensitive enough to give dependable information on such degrees of vitamin C subnutrition as are encountered here.

In his several discussions of the capillary resistance test, Göthlin emphasized repeatedly the fact that conditions other than vitamin deficiency caused fragility of the capillaries, and that the test could be relied upon only when applied to healthy people whose dietary history showed low vitamin C intake. This explains the practice used of procuring medical examinations of all subjects and inquiring into the nature of their diet.

The few college students who reacted with a large number of petechiae were given opportunity for further cooperation by having their vitamin C intake increased through use of several oranges daily. Later when pure ascorbic acid became available both crystals and tablets were used. In some cases improvement resulted in two to three weeks, in others there was no change. A plausible explanation of these differences appeared in the announcement of Szent-Györgyi and associates (20) of the isolation of a vitamin-like substance from paprika and from lemons which reduced capillary fragility. This substance was called vitamin P (permeability vitamin), also citrin, and consisted of two flavones which Wawra and Webb (24) have found to be an equiblibrium mixture of hesperidin and hesperidin chalcone.

In answer to a letter reporting our experiences Szent-Gyögyi sent a small sample of vitamin P. This was administered *per os* in 50 mg. doses daily for two weeks to two subjects whose capillary fragility could not be reduced by large doses of ascorbic acid. The treatment with vitamin P was without effect.

There has been much discussion and many conflicting reports on the effect of vitamin P on permeability of blood vessels. Zacho (27) studied the effect of ascorbic acid and vitamin P (citrin) on the capillary resistance of guinea pigs and observed that the latter increased capillary resistance, but that both citrin and ascorbic acid were necessary for maintenance of normal capillary strength. The hemorrhagic diathesis occurring in scorbutic guinea pigs appeared to be caused by lack of citrin, while the other scorbutic symptoms appeared to develop through lack of ascorbic acid.

Our failure to get results with citrin may thus have been owing to the fact that high ascorbic acid dosage was discontinued during the time citrin was administered. Murlin (18) also found that citrin cured purpura hemorrhagica, but did not cure the form of capillary hemorrhage characteristic of scurvy. He expressed the opinion that the discovery of vitamin P has cleared up many conflicting reports regarding the influence of vitamin C on capillary hemorrhages. Turpeinen (23) expressed the opinion that ascorbic acid cannot be the sole factor controlling capillary resistance, and cited various authorities to show that in human beings vitamin P has frequently been found effective in reducing capillary fragility to normal and in checking a tendency to bleed.

We have not followed up this line of investigation because of the difficulty experienced in finding subjects with marked positive reaction who would be available for investigation over a period of time.

Ascorbic Acid Determination by Urine Analysis. With establishment of the chemical identity of vitamin C, chemical procedures for its quantitative determination were developed.

Liebig in 1824 suggested the idea that nitrogen eliminated in the urine might be considered as a measure of protein matabolism; a similar idea formed the basis of a chemical test for determining ascorbic acid (vitamin C) metabolism in the human subject.

Tillmans and collaborators (21) showed that the antiscorbutic value of lemon juice and other substances paralleled their reducing capacity when titrated with 2, 6-dichlorophenolindophenol. Researchers in nutrition were not slow in adapting the procedure of these workers to determination of ascorbic acid in urine. By this means Harris and associates (11) found that a number of normal individuals showed a fairly constant output of 30-33 mg. of ascorbic acid daily and assumed this to be the normal output for healthy persons. They assigned the term "resting level" (1) to this day-by-day-output on usual diet. They observed also (12) that subjects with a daily ascorbic acid ingestion of 25 mg., considered at that time as the minimum amount for satisfactory nutrition, excreted about 13 mgs. They therefore concluded that an output of less than that amount indicated inadequate dietary ascorbic acid.

Another procedure, employed by itself or in combination with the determination of resting level, was the test dose method. This consisted of administering a single large dose of ascorbic acid and noting the percentage of the dose eliminated in the succeeding 24 hours. With different investigators the test dose varied from 100-1000 mgs., and the percentage return of the test dose that indicated a saturation of tissues varied widely also. In general the percentage return tended to decrease in proportion as the dose increased. Baumann (2) considered a 60 to 80 percent return of ascorbic acid, following a series of 100 mg. doses, to be an indication of tissue saturation. Following a single 600 mg. dose Youmans (26) was of the opinion that a 30 percent return indicated saturation.

Before applying this new procedure to continued study of ascorbic acid metabolism of Utah subjects the nutrition investigators at the Utah Agricultural Experiment Station entered into an agreement with nutrition research workers of four other western states, Idaho, Montana, Oregon, and Washington, to conduct ascorbic acid metabolism studies on a regional basis.

The first year (1937-38) the group undertook study of the state of ascorbic acid nutrition of college women students. The procedure adopted was (a) determination of resting level of urinary ascorbic acid on three succeeding days; (b) the reaction to a single dose of 600 mgs. ascorbic acid. Dietary records were requested of subjects for one week prior to the test, also during the three days of urine collection. At the end of each 24-hour period ascorbic acid was determined by titration with 2, 6-dichlorophenolindophenol. After the third day a 600-mg. test dose was given, the urine was collected during the following 24-hour period and titrated.

In the four cooperating institutions (Idaho did not participate this first year) 170 three-day tests were made. Of this number only 16 showed an average output of less than 13 mgs. ascorbic acid per day, the lowest level of excretion considered to indicate the minimum of satsfactory intake. Slightly more than one-half of the subjects showed a daily average output of less than 30 mgs. These were below the normal standard of Harris, *et al.* By the Youman standard of tissue saturation the majority of this group became saturated following the 600 mg. test dose, since only 7 percent of the group failed to return more than the minimum 30 percent of the dose within 24 hours. If we recognize the probability of three levels of requirement (a) that which is physiologically indispensible, (b) that which is adequate, and (c) that which is optimal, the majority of the subjects were probably ingesting more than the physiological minimum but were not quite reaching the adequate level.

This assumption is strengthened by the nature of the dietary information collected the week prior to, and during the three-day collection period. The main vitamin-C rich foods available locally at the time, namely, citrus fruits, tomatoes, raw cabbage, and canned strawberries, were served an average of only seven times in the 10 days. Use of other fruits and vegetables, both raw and cooked, averaged about one each meal.

Average daily ascorbic acid output of the Utah subjects was more variable than was true of subjects in the other cooperating states. The explanation probably lies in the fact that the Utah group was less homogeneous than the others in two respects, (a) distribution on the basis of academic rating, and (b) type of residence. While Utah students were somewhat unevenly distributed among the four classes, with graduates forming the second largest group in point of number, all Montana subjects and 88 percent of those from Washington were freshmen; distribution of Oregon students was more like that of Utah. Among Utah students ascorbic acid output increased with academic class, freshmen averaged 22, sophomores 48, juniors 51, seniors 97, and graduates 113 mgs. daily.

On the basis of residence Utah students were distributed among boarding houses, bachelor quarters, and homes in groups of three or four at most, while group-living in dormitories or student cooperatives was usual in the other states. Since the amount of vitamin excreted in the urine is a direct reflection of the dietary intake (Nutr. Rev. 1:193

Feb. 1943), the varied intake of students of different academic classes and in different types of residences could well account for the wide variation in resting levels of the Utah subjects.

Ascorbic Acid Determination by the Blood Plasma Method. With development of micro methods for determining ascorbic acid in blood plasma, many research laboratories adopted the blood plasma procedure largely to the exclusion of the more tedious urinary titration method. It had also the advantage of fewer substances which reacted with indophenol, thus complicating results. McLester (15) states a widely accepted opinion to the effect that figures obtained from fasting plasma are more dependable as an index of vitamin C nutrition than an examination of 24-hour urine. In view of this opinion and because of the many difficulties encountered in the urinary analysis procedure, the Northwest Nutrition Research Group adopted the blood plasma method for its second cooperative study of ascorbic acid metabolism. Both men and women students served as subjects.

Because ascorbic acid is not "stored" in the ordinary sense of the word samples were at first taken before breakfast. Since student subjects often traveled a mile or more in order to reach the laboratory it was necessary to learn whether satisfactory samples could be taken at times other than before breakfast. Todhunter, Robbins, and McIntosh (22) of the Washington Experiment Station, made tests of blood plasma ascorbic acid concentration at intervals of one half hour following a breakfast containing no ascorbic acid and concluded that such a breakfast did not affect concentration of ascorbic acid in the blood. Nutrition workers at the Utah Station ran parallel tests on the same subjects, one on fasting blood and one on blood taken within one half hour after a breakfast of scrambled eggs and toast. The correlation was 0.98. Thereafter samples were taken at the Utah laboratory either before breakfast or within one-half hour after a breakfast containing no ascorbic acid.

At the five cooperating institutions a total of 471 women students and 342 men were given blood plasma tests. All four college years were represented and a few graduates were included. Five types of living quarters were recognized: (1) bachelor apartment, (2) dormitory, (3) fraternity or sorority house, (4) home or boarding house, and (5) student cooperative houses; the latter in all states except Utah.

Most authorities agree that a plasma concentration of 0.6 mg./100 ml. marks the lowest level of "safe" ascorbic acid matabolism. A little less than one-fourth of the women subjects (24.4 percent) and more than one-half of the men in this study (55.5 percent) were below this level. The mean value for all women was 0.797 ± 0.0123, practically 0.8, generally accepted as the lowest index of "satisfactory" ascorbic acid nutrition. The average value for all men was 0.59 ± 0.014, just under the "safe" average 0.6. One milligram per 100 milliliters of blood plasma is accepted as the lowest figure indicating tissue saturation. Almost one-fourth (24 percent) of the women subjects but only 7 percent of the men reached this figure. Conversely, only

8 percent of the women and more than one-fourth of the men (27 percent) were in a seriously low state of ascorbic acid nutrition, having plasma concentrations less than 0.4 mgs./100 ml.

Wortis *et al* (25) reported six cases of clinical scurvy with blood plasma ascorbic acid concentrations of 0.22 to 0.30 mgs. While a considerable number of men in this study showed as low ascorbic acid concentrations as did these scurvy cases no symptoms of frank scurvy were in evidence. One young woman with a plasma ascorbic acid level of 0.41 mgs. had badly inflamed gums, which began to heal after two weeks' daily intake of 200 mgs. ascorbic acid.

Analysis of data on the basis of residence showed that women living in student cooperative houses, in those states where they existed, had a mean plasma ascorbic acid value significantly higher than that of any other residence group. In Utah, women living at home showed the best state of ascorbic acid nutrition. Other residence groups (considering all five institutions) were, in the order of quality in ascorbic acid nutrition, homes, boarding houses, dormitories, and sororities.

Men living in homes or boarding houses constituted the only group of men having mean plasma ascorbic acid values significantly higher than the mean for all men. The 104 Utah men were distributed fairly evenly as to numbers in four residence groups. On the basis of blood plasma ascorbic acid below the 0.6 mg./100 ml. level, men living in fraternity houses showed the poorest state of nutrition, those in boarding houses the best.

Grouped on the basis of academic class, freshmen and junior women in all cooperating institutions had mean ascorbic acid values lower than the mean for all women, though the mean for juniors was only slightly lower. Sophomores and seniors had relatively high values. More than one-half (58 percent) of the 151 Utah women were freshmen and an additional 11 percent were juniors, which doubtless accounts for their having an average level lower than was found for the women of the other states. Senior men had higher mean ascorbic acid values than did the other academic classes.

While in all cooperating institutions ascorbic acid levels of men students were generally lower than those of women, the difference was less marked in Utah than in the other states. Even here, however, the difference was significant. In one group of Utah students consisting of 104 men and 102 women, distribution of blood plasma levels showed one-tenth (10.5 percent) of the men and more than one-fourth (28.4 percent) of the women at saturation level (1.0 or more mg./100 ml.); at the "satisfactory" level (between 0.8 and 1.0 mg.) were 17.0 percent of the men and 21 percent of the women; at the "safe" level (between 0.6 and 0.8 mg.) were grouped one-fifth of each; below the lower limit of "safe nutrition" (0:6 mg.) were one-half (52.0 percent) of the men and slightly less than one-third (30.4 percent) of the women.

Other factors which might be considered to cause differences in plasma levels, such as season of the year and age, were submitted to analysis of variance but no difference other than that of sex was significant. Other investigators have reported marked ascorbic acid deficiencies in groups of young men. Borsook (4) reported 1,140 male aircraft workers in southern California, between 18 and 39 years of age, more than one-half (52.4 percent) of whom showed plasma ascorbic acid levels below 0.6 mg., and nearly three-fourths below 0.8 m. Manning (16) reported that 84.9 percent of 782 young men at a National Youth Administration Work Center had plasma ascorbic acid levels below 0.6 mg. If these young men are representative of their population group the situation with respect to their ascorbic acid nutrition may be serious from the standpoint of public health.

It was evident in each phase of these studies that marked differences existed in individual metabolism of ascorbic acid, hence a number of experiments on small groups was made in an attempt to find some of the factors responsible for this variation.

Göthlin (8) based his estimate of the human daily requirement on intake per kilogram body weight. Goldsmith (10) mentioned weight, exercise, and even obesity as possible factors. Belser *et al* (3) found rough correspondence between basal metabolism and amount of vitamin C required to maintain saturation.

At the Utah laboratory practically all students tested by either of the chemical procedures were measured for height, weight, basal metabolic rate, and blood pressure. Plotted against urinary output or blood plasma ascorbic acid none of these factors showed significant correlation. In one group of 85 men whose weight ranged from 115 to 230 pounds, a man weighing 120 pounds had the highest blood plasma concentration and one weighing 200 pounds had the lowest. In this group the highest average blood plasma ascorbic acid values were found among men weighing 120 to 143 pounds. Men weighing more had generally lower averages.

Since weight *per se* was not found to be associated with plasma concentration of ascorbic acid, an index of body build involving both weight and height was plotted against blood plasma ascorbic acid values but no relationship appeared. Ascorbic acid is believed (15) to act as an enzyme or coenzyme in the transport of hydrogen in the body cells. It is possible, therefore, that if some figure representing total amount of active tissue could be found such a value might be correlated with ascorbic acid metabolism.

Finding the amount of ascorbic acid necessary to bring students with low plasma concentrations to a state of tissue saturation was the objective of several experiments. One such study at this station included a group of 10 students, 5 of whom had blood plasma levels below 0.4 mg./100 ml., the other 5 had values between 0.4 and 0.5; all were given 200 mgs. ascorbic acid daily for 8 days. No change was made in their usual diet. At the end of the 8-day period all those who began with a plasma level above 0.4 had reached tissue saturation, (100 or more mg./100 ml.) none of the others had reached that point but concentrations had increased by 70 to more than 100 percent.

One young woman who showed marked vitamin C subnutrition was given ascorbic acid up to 300 mgs. daily and tested at two week intervals from January to June without satisfactory improvement. She was sent to the college physician for examination and learned that her tonsils were badly infected. A test made one month after removal of tonsils showed a satisfactory vitamin C standard. Two other similarly refractory subjects reacted normally after discontinuing use of drugs, thyroxine in one instance, and aspirin in the other.

If we assume that tissue saturation is the desirable state of ascorbic acid nutrition, then we must revise the usual recommendations as to required intake. Ralli *et al* (19) found that 100 mg. intake was necessary to maintain saturation in adult subjects. In our own laboratory we found two women students who, when brought to saturation, required a daily intake of between one and two mgs. ascorbic acid per pound of body weight to maintain that status. Belzer *et al* (3) found that 70 to more than 100 mgs. ascorbic acid daily were required by normal adults to maintain tissue saturation. The recommendation of the National Research Council for maintaining normal nutrition is 75 mg. for men and 70 mg. for women. In view of the studies just reported it may be questioned whether these amounts could be relied upon to maintain saturation.

SUMMARY AND OUTLOOK

DATA have been presented to show that a year's dietary reported by farm families scattered widely over the state was deficient in iron, in phosphorus, and in animal protein, owing to inadequate use of foods that could be readily supplied by the farm. The same deficiencies existed in the dietaries of 891 elementary and 81 high school pupils; the vitamin content of the diet reported by a large group of children was inadequate to prevent scurvy in guinea pigs and to sustain normal growth of laboratory animals. Data presented appear also to warrant the assumption that the diet was inadequate to promote maximal growth in children. Data obtained by two approved chemical procedures have also been presented to show that large numbers of college students were in a state of subnormal vitamin C nutrition. Doubtless many students would recognize the symptoms of subacute scurvy described by McLester (15) viz. listlessness, lack of energy, both mental and physical, failure of appetite, irritability, and pallor. "Fortunately for man," he continues, "clinical experience indicates clearly that between optimal health and frank scurvy there is a wide borderline of deficiency." Fortunately also, it is possible to exist on low ascorbic acid metabolism for a long time before frank scurvy appears. Crandon *et al* (5) report one case in which a man showed a blood plasma concentration of zero for 93 days before the appearance of clinical symptoms.

For the future, nutrition workers at this institution think that the study of nutritional status of human beings should be extended to groups other than those already studied, and to factors other than vitamin C. Rapid progress has been made in connection with determination of the other vitamins; according to Nutrition Reviews (Feb., 1943) the amount of vitamins, with the exception of vitamin A, excreted in the urine is now a fairly direct reflection of the serum content and of the dietary intake. A second line of investigation should include study, with human subjects, of the ascorbic acid value of Utah fruits and vegetables. Looking into the future with the faith inspired by the progress man has already made toward understanding his nutritional needs and their relation to his maximum well-being and power to accomplish, one sees the falling of one after another of the barriers that have retarded progress as new methods of work and unheard-of equipment emerge. Significant trends are seen. Supplementing dietary studies on human subjects, analysis of urine and blood values, and recognition by clinicians of gross lesions caused by nutritional deficiencies, we now have the biomicroscope by means of which the clinician can detect minor lesions in *living tissue,* even as the pathologist is able to detect slight lesions in postmortem tissue.

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