the appetite of their animals. These substances need be present in only minute quantity, but their presence is essential. It is this relation to appetite and food intake that prompts this report.

In the course of certain studies on bacterial nutrition it became of interest, at one time, to test the basal ingredients of culture medium of organic origin, i. e., peptone and beef extract, for their vitamin content. This research was especially indicated, since the literature is not clear on this point. Bayliss,⁷ in his discussion of the growth promoting principle "Bios," says: "It is present in Liebig's meat extract and commercial peptone." Funk⁸ reports the presence of vitamin in meat juice and meat extract, and Osborne and Mendel⁴ as well found "a small amount of the water soluble food hormone" in meat extract.

EXPERIMENTAL METHODS USED

The tests were carried out on young rats, weighing from 50 to 75 gm., which were failing to grow on a diet known to be adequate to promote growth at a normal rate when sufficient vitamin B was supplied. The food mixture consisted of casein, 18 per cent.; sugar, 17; starch 52.5; butter fat, 10, and salt mixture, 2.5. Inspection shows this mixture to be adequate except for the deficiency of vitamin B.

The peptone and beef extract were added to this ration in place of definite quantities of starch. Each substance was tested in the amount of 2.5 and 7.5 per cent. of the ration.

RESULTS

In no case was the decline of the experimental animals stopped by the addition to the ration of definite quantities of either peptone or beef extract.

Chart 1.—Failure of rats that had declined on a diet deficient in vitamin B to recover when beef extract was added as a source of this factor.

The accompanying charts show typical growth curves of rats fed this experimental ration. The initial period of decline, on a diet deficient in vitamin B, is indicated by the dotted line. Following this is the period when the animals were fed the same basal ration plus the

peptone or beef extract and failed to recover; and finally there is the period of recovery, indicated by the rapid rise of the growth curve when the basal ration was supplemented by wheat germ as a known source of vitamin B.

Chart 2.—Failure of rats that had declined on a diet deficient in vitamin B to recover when peptone was added as a source of this factor.

CONCLUSIONS

Commercial beef extract and peptone are devoid of the water soluble vitamin B.

NOTE.—The importance of these observations in connection with the use of beef extract in convalescence will be recognized by all who heard Dr. Mendel at the recent Congress of American Physicians and Surgeons in Washington describe the relation of vitamin B to appetite and food intake.

THE PRACTICAL APPLICATION OF THE RESULTS OF VITAMIN STUDIES

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Our knowledge of vitamins has given a new basis for the evaluation of foods. Certain articles which, from the point of view of their energy value, are almost worthless have been shown to possess great nutritive value. Their importance is not suggested by their chemical analysis. They furnish something very essential in a human diet.

The tomato, cabbage, spinach, lettuce, chard and all the green or leafy vegetables are composed chiefly of cellulose, water and inorganic salts. Fruits have sugar, vegetable acids, water and salts, but none of these things suggest their essential value as foodstuffs.

Many of our foods we no longer eat in their natural state. The conditions of modern life have made necessary the transportation of foods for long distances and the preservation and storage of food in immense quantities for long periods. A certain amount of injury is done to our vegetables, fruits, milk, meats and grain by the processes to which they are subjected in preparation, preservation and storage. The study of vitamins has helped us to understand, to some degree at least,

7. Bayliss, W. M.: Principles of General Physiology, 1915, p. 260.
8. Funk, C.: München. med. Wchnschr., 1913, p. 2614.

the nature of that injury. Some of it is due to the heat applied during our ordinary processes of cooking; some is a consequence of heat applied for purposes of sterilization, whether for the destruction of the germs of disease or for the preservation of food.

We have also sacrificed something in their nutritive value by the refinement of our foods, as in polishing rice and using only the white flour of our wheat to make our bread, and feeding to pigs and cows the balance of the grain. The coarse black bread of the middle ages and of the European peasant of today is despised by our modern civilized city dweller.

But let us not at the same time forget the immense benefits of the preservation and storage of food. Take, for example, the question of white wheat flour. As long as wheat was grown and milled, as it still is in most European countries, within a comparatively short distance of the place where it was consumed, and was used within a few weeks of milling, the problem was a simple one. At present much of our milling is done 1,000 or 2,000 miles from our large centers of population. Not only must the time required for transportation be taken into account, but also the necessity for storage of immense quantities as a normal food reserve. New York City, for instance, consumes more than 20,000 barrels of flour every day. Much of this, it is estimated, has been milled five or six months before it is eaten. White wheat flour keeps indefinitely, certainly for many months, without any important deterioration. But whole wheat flour can be kept only about thirty days; after that it is likely to become "wormy." Flour experts tell us that the general adoption of whole wheat flour for bread in this country is an economic impossibility. The modern method of milling and our system of transportation and storage make a bread famine here almost impossible.

Although heating milk may injure or destroy its vitamins, this fact does not invalidate its great advantages, such as protection from diseases which may be communicated through milk and its preservation by drying, condensing or sterilizing, which permits its wider use as a food all over the world. The same may be said of the canning and drying of vegetables, fruits and eggs. These preserved foods are all of great benefit in the nutrition both of children and of adults. We would not stop the use of them if we could.

Our knowledge of vitamins has, however, pointed out that these procedures have their disadvantages, even their dangers; but when the nature of these is once thoroughly understood and their importance appreciated, the remedy will come also.

In the food of infants it is only vitamin C that is likely to be injured by any process to which their food, chiefly their milk, is subjected in preparation or preservation. In the first place, it should be understood that the amount of this vitamin in milk is small. Chick and Hume found that, to protect a guinea-pig, whose food contains no other source of this vitamin, 100 c.c. daily of fresh milk is required, although complete protection is secured by only 1.5 c.c. of orange juice.

It is well established that all heating of milk (I do not, of course, mean warming for feeding) whether by boiling, pasteurizing, sterilizing, drying or condensing, injures this vitamin. It has not been shown that vitamin A or vitamin B in milk is thus injured. The amount of injury done to vitamin C depends on the height of the temperature and the length of the period during which the temperature is maintained, and pos-

sibly on whether the heating is done in open or in sealed vessels. The duration of the heating seems clearly more important than the temperature employed. Short heating at a high temperature apparently does less injury than prolonged heating at a lower temperature; so far as its effect on this vitamin is concerned, boiling for five minutes seems better than pasteurizing for thirty minutes.

While there is still considerable difference of opinion among investigators as to the relative amount of damage done by various types of heating, it may be regarded as proved that they all injure milk in this respect, and that the only safe rule in practice is to supply some efficient antiscorbutic in the diet of all infants reared on milk treated in any one of these ways.

Evidently the body has a sufficient store of this vitamin to meet its needs for a considerable time, for symptoms of scurvy do not usually appear for some months after the deficient diet has been taken. Of the last nine cases of infantile scurvy treated in my hospital service, the period was between five and seven months in seven, and in none more than nine months.

If the food contains even a small amount of antiscorbutic vitamin, the development of scurvy will be delayed. To infants whose principal or sole food is any one of the forms of heated, dried or condensed milk, it would appear, then, to be quite sufficient if an antiscorbutic were begun at the age of 5 months.

The observations of Hart, Steenbock, Ellis and others indicate that the vitamin content of cow's milk is affected by the food of the animal. This was first shown to be true of the vitamin C. The winter milk of stall-fed animals was decidedly poorer in this respect than the summer milk of pastured animals. The same law seems to hold with respect to all the vitamins. If the food of the cow does not contain an adequate supply, the milk may be deficient in any or in all of them. It would seem, therefore, a wise precaution during the winter to supplement cow's milk by other foods known to be rich in this vitamin, such as the yolk of egg or the juice of steamed green vegetables, but best of all by cod liver oil.

The vitamin content of the food of the nursing mother undoubtedly affects her milk in a similar way. This may furnish a clue to some of the puzzling cases of scurvy developing in nursing infants.

It is reported that, among the Filipinos, beriberi is common among the nursing children of rice-eating mothers of those islands. This is believed to be a large factor in the extremely high infant mortality that is seen there.

These facts may explain why infants do not thrive on some milks, although the supply is abundant and the proportion of the different constituents, as shown by chemical analysis, is within normal limits.

The practical application of these facts is, first, to recognize the necessity of supplying to nursing mothers a diet which is ample in all the vitamins. Vitamin A and vitamin C are the ones most likely to be lacking in the diet of the poor. These vitamins are abundantly supplied by milk, eggs, green vegetables and fruits, all of which unfortunately are expensive foods but should be included in the diet.

I have never seen and have never known of a case of scurvy in a child over 2 years old who was living under normal peace conditions. So far as vitamin A—so indispensable for the growth of children—is concerned, it is necessary only that care be taken that the

diet include an ample supply, since it is not likely to be injured in the preparation or preservation of food.

We know well the dangers of vitamin deficiency when the diet is necessarily restricted, because conditions do not admit of choice or variety of food. These conditions exist in times of famine or great food shortage, or even may be the result of poverty; also in prisons, army camps, on shipboard, in the arctic regions and, one must add, in infancy. The consequences to children are serious, whether we consider simply arrested growth and general malnutrition or the diseases, such as scurvy and beriberi, which result from marked and prolonged deficiencies. But it does not seem probable that, except in conditions like those mentioned, either children or adults who take the average or usual diet are likely to receive such small quantities of the vitamins as definitely to interfere either with growth or normal nutrition.

A glance over the list of foodstuffs known to contain the different vitamins shows how abundant vitamins are in most common foods. This may be one of the reasons why, in the evolution of the diet of the human race, certain foods have a place. It seems perfectly evident that, unless the diet given is a very one-sided one, children receive in their usual food a liberal supply of all these essential food constituents.

Two very striking things are brought out in the investigation of vitamins by observations on animals: One is the very small amounts which are apparently required to produce their effects, and the other is the specificity of their action.

Until these substances have been isolated, we shall not know the amounts required for normal nutrition. Apparently, the amount of any one of them is not large.

Chick, Drummond and their associates at the Lister Institute have shown how much of different foods is required to protect laboratory animals against beriberi and also against scurvy, when the diet contained no other source of the vitamin in question. While this establishes much that is important with regard to the relative value of foods, it gives us no idea as to the actual amounts required by human beings. All the evidence goes to show that the vitamin requirement is affected by many conditions. It undoubtedly varies even in animals. Laboratory animals in confinement might be expected to show effects of deficiencies in diet sooner than those living under natural conditions. It is well known that men who were much exposed and doing hard work were affected by scurvy sooner than others, although all had the same diet. If the human diet is poor in other respects, the effects of the absence of the antiscorbutic or any other vitamin is more quickly apparent.

How much of the different vitamins is needed for health we do not yet know. It is clearly not a definite amount for all human beings of the same age, sex and weight; but, like our other food requirements, the vitamin need no doubt varies with many conditions.

The great importance of vitamins for growth makes it imperative that the diet of children especially should contain the articles of food that are rich in these factors. The requirements of adults are for maintenance merely and undoubtedly are much less than those of children. This is especially true of vitamin A.

It is during the period of infancy that children are likely to suffer most: first, since infants are the most susceptible of human beings to all adverse conditions; secondly, infancy is the period of most rapid growth,

and anything which may affect growth produces its most marked effects at this time; and finally, the diet of infancy is necessarily a restricted one.

Proprietary foods are harmful, not so much from what they contain as from what they lack. They may be deficient in all three of the vitamins.

The specificity of action of these substances is quite as great as that of antitoxin in diphtheria or thyroid extract in cretinism. The different vitamins seem entirely independent of one another in their activity. They are in no way interchangeable; they seem to have no relation to one another. We cannot supply a deficiency in vitamin B by giving more of vitamin A, nor can we protect against scurvy by the most liberal allowance of vitamin B. Each one has a perfectly definite function in nutrition, which, from all evidence now in our possession, can be performed by it but by nothing else.

If no vitamin deficiency exists in the diet, it does not seem probable that general symptoms of malnutrition in children past the period of infancy who are taking a varied diet are due to a deficiency of any of these factors, or that improvement in general nutrition is likely to follow their administration in larger amount, when no real deficiency exists. In other words, benefit from an excess of any of them seems most improbable, and we lack proof that such is the case.

Another practical question is whether if the diet is low in its vitamin content, i. e., a condition of relative deficiency exists, there may occur perhaps not frank scurvy, beriberi, rickets or keratomalacia, but milder and less definite symptoms, such as failure to make normal progress in growth, malnutrition and general evidence of ill health. This is something difficult to establish. On *a priori* grounds it seems not improbable. It must be remembered, however, that symptoms such as those mentioned may be due to a great variety of causes other than vitamin deficiency. In the absence of definite means of diagnosis, the only evidence of their dependence on vitamin deficiency is the therapeutic test, namely, prompt and decided improvement, which follows when foods known to be especially rich in the different vitamins are added to the diet—such as orange juice or yeast or cod liver oil.

Reasoning from experience with deficiency diets in animals, one would expect to see improvement in a few weeks. In this connection one is reminded of the "patent medicine" advertisement which ran somewhat as follows: "If you are not cured you haven't got the disease. The remedy never fails."

It should first be evident from an analysis of the diet that a deficiency probably exists. The changes made should be as carefully planned as are laboratory experiments with rats or guinea-pigs. Otherwise the results reported to follow are likely to depend on either the faith or the skepticism of the observer.

Some suggestive observations on the use of antiscorbutic vitamin have been made by Hess and others, in which the weight curve of infants showed a prompt rise on addition of orange juice to the daily diet; but in many or most of these cases the diet was known, or at least strongly suspected, to be poor in this factor.

Vitamin B has been urged upon the profession in the form of yeast as being especially important for children who are not making the normal gain in weight, who suffer habitually from poor appetite, chronic constipation, etc. My own experience has been one of complete disappointment.

However, in view of the important part which we now know to be played by vitamins in nutrition, it behooves the physician in all cases of malnutrition, particularly when the explanation is not obvious, to investigate carefully the character of the food and its preparation to discover any errors that might result in a vitamin deficiency. Especially is this necessary in the case of chronic invalids or of delicate children whose diet has become greatly restricted from necessity or from caprice, and in the case of infants, whose diet is always a restricted one. But, until we have some more certain means of diagnosis than we now possess, the indiscriminate use of vitamins in other circumstances than the foregoing for what is often referred to as "general results" is not likely to be beneficial; it should be discouraged. It is hardly scientific therapeutics.

It is most unfortunate that the popular interest in vitamins, which is the result of so much recent publicity as has been given to this whole subject, should be exploited commercially. Just now vitamins are in fashion, and as much capital as possible is being made of this fact. The medical profession, at all events, should not be carried along in the popular current. Important and indispensable though vitamins are, one can fall into no greater error than to assume that vitamin deficiency is the chief cause of all chronic nutritive disorders; just as not very long ago these were all referred to auto-intoxication, and at present a certain group would have us believe that they are due to some disturbance of the glands of internal secretion. The use of vitamins without definite indications will be popular for a period but, like other fads, it will pass. With time and further investigation, their true place will be determined.

Our knowledge of vitamins has taught the necessity of a variety of food and the danger which follows when conditions make a choice of variety impossible. It has taught us also the incomparable value of certain foods, particularly of milk, not only in infancy, but during the entire period of growth; also the importance in the diet of children of the green or leafy vegetables. The chief objection to some, such as cabbage, lettuce and celery, when used in a raw state is the difficulty of making children masticate them properly.

Our knowledge of vitamins has greatly helped to put the whole subject of nutrition on a scientific basis. The experimental method has been substituted for the empiric one in determining the value of the different foods. Formerly we might know that certain foods were desirable or necessary; now we are able in very many cases to say why such is the case and to determine their precise value in nutrition. A knowledge of vitamins has furnished a key to many problems in nutrition which before were obscure or insoluble.

Until they have been confirmed by clinical experience there is, however, some danger in relying too much on the results of laboratory observations on animals of a different species, whose physiologic needs may be different from those of human beings.

The study of vitamins has taught us several important things regarding the nutrition of children.

Children should eat a variety of food, and special dangers may follow the habitual use of a very restricted diet.

Milk is the one indispensable food for children. The diet during the entire growth period should include, if possible, whole milk, or if skimmed milk is used it should be supplemented by butter. Of the butter sub-

stitutes, those which contain beef fat, mutton fat and peanut oil are better than those in which other vegetable oils or lard are important constituents.

A diet which includes no milk whatever should contain ample amounts of the green or leafy vegetables.

Cereals, particularly those from whole grains, and potato are important and adequate sources of vitamin B.

Fruits have other uses than as laxatives and as sources of mineral salts; they should form a regular part of the diet. When fresh fruits are not available, dried fruits may be given; but they are distinctly inferior to canned tomatoes as sources of the antiscorbutic vitamin.

Cabbage is such a rich source of all the vitamins that it should form a larger part of the diet than is usually the case, especially since it is cheap, and in winter often almost the only green vegetable available.

In normal peace conditions, the results of vitamin deficiency are most often seen in infancy. In rare cases they may be seen in older children and in adults when there is extreme poverty, and still less frequently in those suffering from chronic disease, or in very delicate children whose diet for a long period has been greatly restricted.

If the daily diet contains in reasonable amount unskimmed milk, cereals, potato, green vegetables and fruit, one need not fear a vitamin deficiency. While these articles are especially rich in vitamins, nearly all of our common foods contain them.

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CLOSTRIDIUM BOTULINUM

II. PRESENCE IN THE HUMAN ALIMENTARY TRACT *

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The importance of *Clostridium botulinum* as a cause of food poisoning, and probably food infection, justifies extensive study of its distribution. At frequent intervals it has been reported in the intestinal contents of both apparently healthy and diseased animals and human beings. The present paper is a report of a short study on its possible presence in the intestinal tracts of healthy human beings.

Van Ermengem¹ isolated the organism from the intestinal tracts in fatal cases of the disease. In 1897, however, he could not find it in the intestinal contents of fish, or in cow or horse manure, or duck excreta. Burke² found the spores of this organism in insect droppings and manure from a hog which had recovered from botulism three months before. Dickson³ examined the intestinal contents of 250 hogs without finding the organism in a single instance. Kempner and Pollack⁴ isolated it in 1897 from the intestinal contents of a hog. We⁵ found it in three specimens of hog feces and one sample of sewage. Graham and Barger⁶ found *Clostridium botulinum*, Type A, in one specimen of feces and five specimens of urine from

* From the Department of Bacteriology, University of Illinois.

1. Van Ermengem: Centralbl. f. Bakteriöl., Part I, **19**: 442, 1895.

2. Burke, G. S.: J. Bacteriol. **4**: 541-553 (Sept.) 1919.

3. Dickson, E. C., quoted by Burke (Footnote 2).

4. Kempner and Pollack: Deutsch. med. Wchnschr. **23**: 505, 1897.

5. Tanner, F. W., and Dack, Gail M.: J. Infect. Dis., to be published.

6. Graham and Barger: Univ. Bull. **19**, No. 7, 1921.