A BRIEF DISCUSSION OF VITAMINS A, B, C, AND D

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It is impossible in an article of this nature to adequately cover the field of the vitamins, but at least some idea can be given of their history, properties, uses and occurrence.

For many years it has been known that a food to be nutritionally adequate for all needs of humans or animals must contain the proper amounts and kinds of carbohydrates, proteins and fats, besides mineral elements (for bone formation) and water. As laboratory methods improved and direct experimentation with animals took the place of theories it began to be observed that the purer the foods fed the shorter the length of life of animals kept on artificial diets. As early as 1843 Peckelharing [1] stated:

"When mice are fed on bread baked with casein, albumin, rice flour, lard and a mixture of all the salts which ought to be found in their food, while they are only given water to drink, the animals starve to death. During the first few days all is well. The bread is eagerly nibbled and the mice look healthy. But soon they get thinner, their appetite diminishes and in four weeks all the animals are dead. If, however, instead of water they are given milk to drink, they keep in good health, though the quantity of albumin, lactose and fat which they assimilate with the milk is quite negligible in comparison with what the bread on which they are fed contains. The element in the milk which keeps the animals alive also occurs in the whey from which the casein and fat have been eliminated. Till now my efforts constantly repeated during the last few years, to separate this substance from the whey and get to know more about it, have not led to a satisfactory result, so I shall not say any more about them. My intention is only to point out that there is a still unknown substance in milk, which, even in very small quantities is of paramount importance to nourishment. If this substance is absent, the organism loses the power properly to assimilate the well-known principal parts of food, the appetite is lost and with apparent abundance the animals die of want. Undoubtedly this substance not only occurs in milk but in all sorts of foodstuffs, both of vegetable and animal origin."

This clear-cut recognition of some unknown but essential factors in nutrition escaped general notice since it was published in Dutch, and it was not till 1906 that Hopkins in England made note of the fact that synthetic diets failed to support growth unless a little milk or certain vegetables were present. In 1912 [2] he published a more complete work proving the presence in butter of an unknown substance that was necessary for growth. Osborne and Mendel [3] obtained like results in the same year, and shortly after they discovered

simultaneously with McCollum and Davis,[4] two unidentified substances upon which the growth of rats depended. These were known as the "fat-soluble" substance and the "water-soluble" substance, being so named on account of their differing physical properties. Funk[5] in 1913 found a nitrogenous substance in rice polishings that cured beri-beri and because it had chemical properties that made it appear like a class of substances known to chemists as "amines" and was similar or identical with the water soluble substance previously discovered, he believed it to be an amine vital to life and called it a "vitamine". Many workers were now engaged in research on these strange compounds that had such a profound influence on life and for want of better means of identification letters of the alphabet were prefixed to the term "vitamine" for the fast increasing list of separate and distinct compounds that affected the growth or functioning of the animal body. As knowledge of the properties of these substances increased it was found that many of these new vitamines were not basic in character and did not have the properties of amines and to avoid confusion Drummond in 1920 suggested that the final *e* of vitamine be dropped and that the term "vitamin" be used prefixed by some letter to designate the substance under discussion. This has been approved and so now we have a whole alphabet of these strange substances that are so important to our health and welfare. Due to the rapid growth of this new branch of nutrition many terms have been coined for vitamins, based on their physical, chemical or physiological properties, so that the literature is somewhat confusing unless we keep in mind the many synonymous terms. Table 1 will help us in gaining an idea of the names together with a brief summary of effects of the known vitamins.

TABLE 1

Name	Synonyms	Effect of lack of vitamin in diet
Vitamin A. ..	Fat-soluble Antiophthalmic Growth-promoting	Cessation of growth; ophthalmia; weakening of the body tissues; increased susceptibility to infections of several kinds; lung, skin, and bladder infections; inflammations and pus formation in sinuses and sublingual glands.
*Vitamin B. ..	Water-soluble Antineuritic Growth-promoting	Cessation of growth; loss of appetite; weakness; loss of weight; lack of vigor; gastro-intestinal derangements; indigestion, constipation, colitis; symptoms of malnutrition of the nervous system and finally beri-beri; body is weakened and offers no resistance to invading organisms; increased sterility.
Vitamin C. ..	Water-soluble Antiscorbutic	Sallow, muddy complexion; loss of energy; fleeting pains in the joints and limbs, especially in the legs, usually mistaken for rheumatism, finally scurvy; tooth defects; lack of stamina and growth; increased susceptibility to infectious diseases.
Vitamin D. ..	Fat-soluble Antirachitic	Failure of mineral metabolism faulty bone formation, lowering of calcium of blood, possibly increased susceptibility to respiratory infections, rickets.

* Made up of at least two vitamins. Discussed more fully on page 271 of this article.

VITAMIN A

Historically, vitamin A was not the first discovered but was one of the growth promoting substances in milk, along with vitamin B, that first led Hopkins [2] to publish in 1912. Osborne and Mendel [3] found that butter fat added to diets, adequate in all known respects, made the difference between life and death for experimental animals. Without butter fat the rats ceased growing and died. With it they lived and grew in a normal manner.

Though vitamin A is not a specific cure for any disease it is perhaps one of the most important of the vitamins from the standpoint of general health and its absence from the diet paves the way for a large variety of infectious diseases.

When a young growing rat is fed a diet adequate in all other respects but lacking vitamin A, growth continues for a short time, probably because of the previous storage of vitamin A in the body. Then growth ceases and if the diet is entirely devoid of the vitamin, a loss of body weight occurs followed by a condition of general decline leading to death. When the store of vitamin A is used up and growth ceases, the animal shows increased susceptibility to bacterial infection. A large proportion of the experimental animals develop a characteristic disease of the eye, known as xerophthalmia.

Vitamin A is a factor of great practical importance to nutrition and health because a lack of it weakens the body and increases its susceptibility to many infectious diseases; even though vitamin A does not have direct controlling relation to any one disease as does vitamin B to beri-beri and vitamin C to scurvy.

Xerophthalmia involves infection, but it is essentially a deficiency disease because dietary deficiency greatly increases the susceptibility of the animal to the infection and thus practically determines whether or not the disease will occur. If not too advanced it can be cured by feeding the animal a proper amount of vitamin A in the diet. A surplus of vitamin A in the body not only assures the use of it for future time, but greatly increases the ability of the body to resist disease. It must be supplied in liberal proportion during growth and in the food of the adult too so as to insure not only a good condition of nutrition but also increased health and vigor. The demand for vitamin A in the period of reproduction and lactation is even greater than during growth.

Both young and old animals have been shown to be able to store a considerable amount of vitamin A in the body. There is an actual storage of this vitamin in the tissues, although about nine-tenths of

the total vitamin A in the body of a well-nourished adult rat is found in the liver, the remaining one-tenth is equally divided between the muscles, the blood, the kidneys, and the lungs. This ability of the body to store it for future use is sometimes an unfortunate factor, since a lack of A in the diet does not manifest itself immediately and weakening of the body may result before the deficiency becomes evident.

VITAMIN B

Reference to a disease that we now recognize as beri-beri was published [6] as early as 2600 B. C. but it was not till 1880 A. D. that Takaki, surgeon general of the Japanese navy, while investigating an outbreak among the sailors, showed that the disease could be prevented by a change in diet. One vessel on a nine-months' cruise had 169 cases out of 276 men. Takaki commissioned another ship with the same number of men and sent it on an identical voyage. The only thing he changed was the ration, giving less rice and more barley and adding meat, vegetables and condensed milk. Fourteen cases of beri-beri developed and these were among men who had failed to eat the ration.

Other workers soon proved that the eating of polished rice led to the disease and that the substitution of unpolished rice was sufficient to prevent or cure the disease.

Funk [5] 1911 isolated a very potent anti-beri-beri substance from rice polishings which he called a "vitamine", which term, less the final e, we now use as a generic title for all the substances which exert such a profound influence on health.

Vitamin B is the name generally applied to the substance which prevents beri-beri. Since beri-beri is a nerve disease, a so-called neuritis, the substance which prevents it was designated as antineuritic. Beri-beri results from too great a dependence upon polished rice as a food and can be prevented by the use of unmilled rice or of the parts of the rice which have been removed in the milling, particularly the embryo. At the time of its discovery the substance was proven to be water-soluble and growth promoting. Vitamin B is the term now used to cover the chemical individual or group whose presence in food enables it to meet the needs of the body in preventing disease and supplying the substances essential to growth.

The animal organism cannot store this vitamin in sufficient quantities to be able to go without a supply of it for any length of time. The amount needed increases as the body increases in size, being highest during reproduction and lactation.

In mammals a deficiency of vitamin B in the diet causes a loss of appetite commonly followed by more complex and less clear symptoms than in the case of birds. These symptoms are grouped by McCarrison under the order of "malnutrition, derangement of the functions of the organs of digestion and assimilation, disordered endocrine function, and malnutrition of the nervous system." A partial but not complete deficiency in this vitamin leads to impaired growth and a general undermining of health and vigor. This lowered vitality may have a far-reaching effect in its influence on reproduction and successful rearing of the young. While often referred to as growth-promoting it should be emphasized that vitamin B is essential to normal nutrition at all ages.

Vitamin B is probably a nitrogenous base relatively stable to oxidation and to heat and is evidently more stable in acid than in alkaline solution. Little heat destruction occurs in ordinary cooking, but in commercial canning and sterilizing due to the higher temperature involved, the losses might be more serious. In ordinary cooking, losses of vitamin B are more likely to occur on account of its solubility in water and the consequent loss by extraction if the cooking water is rejected, than through instability to heat at cooking temperatures. The distinguishing features of vitamin B when compared to vitamins A and C is the effect of its greater stability which tends to make the problem of its ultimate isolation and identification a more hopeful one than that of vitamin C with its marked susceptibility to heat, to alkalinity and to oxidation. At present the evidence leads us to believe that B is made up of two vitamins.

THE MULTIPLE NATURE OF VITAMIN B

The question of the multiple nature of vitamin B is still a subject of research. If the investigators who are now working on this problem can prove the multiple nature of this vitamin (the antineuritic and growth promoting factors), they would accomplish a great deal indeed for the advance of the chemistry of food nutrition.

In 1920 [7] Emmett and Luros carried on a series of elaborate experiments in which they employed both pigeons and rats. They offered a tentative conclusion that the antineuritic substance as tested for, by pigeons, and the water-soluble B tested for, by rats, were not the same, and that it would be better to consider them as being different until further proof was forthcoming.

Funk and Dubin [8] (1921) reported that what had been called vitamin B consisted of a mixture of two vitamins: (1) the anti-

neuretic substance readily removed from autolyzed yeast by absorption upon fuller's earth, and which they proposed to call vitamin B; (2) the water-soluble substance less readily absorbed by fuller's earth and exerting a specific growth-promoting influence upon micro-organisms and which they proposed to call vitamin D.

Smith and Hendrick[9] (1926) reported experiments which are very significant indeed because they throw some light on this subject. They found "that 14 per cent of rolled oats as the only source of vitamin B, supplemented with purified food-stuffs and vitamin A, failed to induce satisfactory growth in rats. The addition of 2 per cent of dried brewer's yeast gave a better growth curve." They tried supplying the protein both in the form of gelatin and casein but neither of the two stimulated growth as did the yeast. From this observation they inferred that it was not the protein of the yeast which supplied the nutrient principal lacking in the oats. They autoclaved the yeast at 15 pounds pressure for six hours and then showed that this treatment completely destroyed its power to induce a growth response under the former conditions. It has been repeatedly reported that autoclaving yeast destroys the antineuretic substance.

At the same time that Smith and Hendrick were working on the problem, Goldberger[10] and associates carried on similar investigations and reported experiments (1926) which demonstrated the same thing. They found "that 27 per cent of autoclaved yeast failed to serve as a source of what has been called vitamin B when employed in a purified diet supplemented with fat-soluble vitamins. On the other hand the diet of purified food stuffs plus the fat-soluble vitamins A and D, and containing the corn extract equivalent to 5 per cent of corn in the diet, together with 8 per cent of autoclaved yeast, induced essentially the normal rate of growth." They also found that beef contains the same factor which autoclaved yeast has and which gives it its supplementary value with respect to the corn extract.

Both dried yeast and fresh beef have preventive or curative action in pellagra when the amounts fed are insufficient to prevent the appearance in human subjects of incipient signs of beriberi. Goldberger has named this heat-stable substance in yeast and in lean meat which acts as a nutrient supplement and prevents pellagra, P–P.

Sherman and Axtmayer[11] working on this problem of the multiple nature of vitamin B used yeast and whole wheat. They found

that autoclaved yeast contains the antineuritic factor while whole wheat also contains the antineuritic factor but not the pellagra preventing (or P–P of Golberger). The results obtained from the mixture of the autoclaved yeast and the wheat seem to show that the substance furnished by the autoclaved yeast which supplements whole wheat may be a newly discovered vitamin.

After considering all the work that has been done on this subject one can think of vitamin B as a combination of at least two principles: (1) the antineuritic substance, and (2) the water-soluble growth-promoting substance, the so-called P–P.

VITAMIN C

Scurvy once called "the sailors' scourge" has been known for centuries and written record of it has come down from the time of the Crusades.

Various theories have been held as to the origin of the disease but the two which gained most ground were the infectious and dietary.

By 1795 the British navy had become so convinced of the efficacy of lime juice as a curative measure that it was issued with the ration to all sailors, and scurvy practically ceased on English ships.

In 1849 Budd [12] wrote that scurvy was due "to an essential element, which, it is hardly too sanguine to state will be discovered by organic chemistry or the experiments of physiologists in the not far distant future." Yet 70 years later with all the accumulated knowledge of the vitamins at hand scurvy broke out among troops in the World War.

Vitamin C is the substance which prevents scurvy and has thus been called "the antiscorbutic vitamin". It apparently passes from an inactive substance in the ripe seed to an active form in the germination of the seed (the mature resting seed lacking vitamin C, being particularly rich in vitamin B). This relationship has led to the suggestion that vitamins B and C stand in close chemical relationship to each other. As yet, the experimental evidence in this matter is but rudimentary. Vitamin C is much more readily destroyed than is vitamin B, both by oxidation and heating.

"Among the more readily noticeable symptoms of a vitamin C deficiency, are soreness and stiffness of joints with a tendency to hemorrhages in them, soreness and hyperemia of the gums leading to looseness of teeth, and bone changes."[12] It should be remembered though that the absence of scurvy does not prove that

the food is supplying all the vitamin C that the body requires for the best fulfillment of its physiological functions. Lack of vitamin C increases susceptibility to infectious diseases while ample supplies of vitamin C increases the resisting power of the body. Much of the so-called rheumatism is due at least in a large part to the use of food too poor in vitamin C. Tooth defects are also very often due to a diet low in this vitamin.

Vitamin C like vitamin B is not stored in the animal organism so that the body depends upon food for its daily requirement.

VITAMIN D

Vitamin D has not long been recognized as a separate entity. It is so closely associated with vitamin A in its occurrence that for a long time A was believed to not only cause growth but also influence bone formation.

In 1922 McCollum [13] showed that codliver oil which had been heated for several hours at 100° C and had had a stream of air bubbled through it, no longer was able to cure the ophthalmia of rats on A free diets. Therefore the vitamin A in the oil had been destroyed by heat and oxidation. But this same oil still had the power to cure rickets in rats. This could only mean that there was a new substance that affected bone formation, and it became known as the antirachitic factor or vitamin D.

Empirically, codliver oil has long been a standard medicine and many of the inhabitants of the costal regions of northern Europe eat the livers of fish. It was not, however, till 1913 that sound scientific reason for this practice became evident.

Zucker, Pappenheimer and Barnett [14] in 1921 isolated a potent fraction from codliver oil and then came the astounding discovery made independently by Hess [15] and Steenbock [16] that olive oil and other foods which have no antirachitic properties, could be activated by sunlight or ultra violet light from a mercury arc lamp, so that they had the same curative properties for rickets as codliver oil.

This opened up a great field of research and explained much that was contradictory, in that peculiar disease, rickets. It had long been known that rickets was a failure of the normal metabolism of calcium and phosphorous and that the bones of a growing child with this disease failed to develop normally. It was also known that codliver oil and sunlight exerted a beneficial effect in this disease. Now the various links in the chain were more complete. Codliver oil contained a substance, vitamin D, that regulated calcium

and phosphorous metabolism. Sunlight or ultra violet light produced in oils a substance that acted like vitamin D.

The final step was the proof that certain chemical substances cholesterol or ergosterol which occur in oils and which are inactive as far as curing rickets, become powerfully curative when treated with ultra violet light. Cholesterol or related compounds occur in human skin, and light of the proper wave length falling on the surface of the human body is able to convert part of these compounds into vitamin D. This accounts for the fact that the Rickets Commission [17] which visited Porto Rico last year was unable to find more than one case of rickets in 600 children examined in the Island, living under such conditions that some would have developed the disease if living in northern cities. Our many days of sunshine have protected the children against conditions of poverty and bad food. The sunlight manufactured the vitamin in the body that normally they should have received in their food.

To summarize briefly; from Table 2 we see that many of the foods were tested in the raw state and that where the same article has been tested after cooking we notice a diminution in vitamin C and sometimes in vitamin B. Experimental work shows that in the destruction of the vitamins by heat, oxidation from oxygen of the air plays an important role and that frequently a canned food may contain more vitamin C, for example, than the same food cooked in the home, due to the fact, that chance of oxidation is generally less in steam cooking by autoclaves in the canning factory that in cooking with open kettles in the home. Vitamin C is the least stable and may even be destroyed by standing exposed to air as in the case of milk, which is furthermore very apt to be low in C.

The presence of acids such as exist in lemons, oranges and tomatoes tends to stabilize all the vitamins as they are more susceptible to heat and oxidation in an alkaline media.

Vitamin B is more stable than C and will not be appreciably affected by boiling temperatures for short periods.

Vitamins A and D are the most stable of all and are hardly decreased by boiling but may be destroyed by prolonged cooking of foods in fats and oils.

We should obtain our vitamins from the liberal use of milk, fruits and green vegetables which not only supply these necessary nutritional factors but are excellent foods in themselves and also an important source of the mineral elements.

Animals cannot synthesize the vitamins and must obtain them

from their food. The capacity of the animal body to store them is variable. Vitamin A seems to be stored to the greatest extent and B and C to the least. The milk of cows varies in its vitamin content due to differences in the food. So the milk of the mother may vary and many nursing infants develop scurvy or rickets and other nutritional deficiency diseases due to a lack of vitamins in the milk, direct evidence that the mother's diet is at fault.

Reproduction and the growing period make the greatest demands on a food, if the individual is to be supplied with all the necessary elements for its well being. The necessity of an adequate supply of all the vitamins and mineral salts is most imperative at these times, and the diet should be chosen with regard to these requirements.

TABLE 2

SOME FOOD SOURCES OF VITAMINS A, B, C, AND D

SYMBOLS:

\+ indicates that the food contains the vitamin.
\+ + indicates that the food is a good source of the vitamin.
\+ + + indicates that the food is an excellent source of the vitamin.
— indicates that the food contains no appreciable amount of the vitamin.
? indicates doubt as to presence or relative amount.
* indicates that evidence is lacking or appears insufficient.

Food	Vitamin A.	Vitamin B.	Vitamin C.
Apples, raw	+	+ to + +	+ +
Apples, canned	*	*	— to + +
Avocado (Alligator pear)	+	+ +	*
Bananas	+ to + +	+ to + +	+ +
Beans, kidney	+	+ + +	*
Beans, navy, dry or canned	+	+ + +	*
Beans, string, fresh, raw	+ +	+ +	+ +
Beans, string, cooked	+ +	+ +	*
Beef	+	+ +	— to +
Bread, white, water	?	+	—
Bread, white, milk	+	+	— to +
Bread, whole wheat, milk	+ +	+ +	— to +
Butter	+ + +	—	—
Cabbage, green, raw	+ +	+ +	+ + +
Cabbage, head, cooked	+	+ +	+
Cabbage, head, canned	+	+ +	+
Carrots, fresh, young	+ + +	+ +	+ +
Cheese, whole milk	+ + to + + +	—?	*
Coconut	+	+ +	*
Codliver Oil	+ + +	—	—
Corn (maize) yellow	+ +	+ +	—
Corn meal	— to +	—	—
Eggs	+ + +	+ to + +	—?
Egg plant	+	+	*
Fish, lean	— to +	+	*
Flour, white	—	— to +	—
Grapefruit (or juice)	+	+ +	+ + +
Grapes	+	+ to + +	+
Lard	— to +	—	—
Lettuce	+ to + +	+ +	+ +
Limes (or juice)	*	*	+ +
Mangoes	*	*	+
Meat, canned	— to +	+	—
Milk (whole)	+ + +	+ +	+ variable
Milk, condensed	+ + +	+ +	+ variable
Milk, evaporated	+ + +	+	—*
Milk, dried, whole	+ + +	+ +	+ variable
Molasses	—	+	*
Oatmeal	— to +	+ +	—
Okra	*	+ + +?	*

Food	Vitamin A.	Vitamin B.	Vitamin C.
Olive Oil	— to +	—	—
Onions, raw	— to +	+	++
Onions, cooked	— to +	+	+
Orange juice	+	++	+++
Peanuts	+	++	*
Peas, young, green, raw	++	++	++
Peas, canned	++	++	++
Peas, dry	+	++	?
Pineapple, fresh, raw	++	++	++
Pineapple, canned	++	++	++?
*Plátano	++	+	*
Pork	— to +	+++?	—
Potatoes, sweet	++	++	++
Potatoes, white, raw	+	++	++
Potatoes, white, boiled one hour	+	++	+
Potatoes, white, baked	+	++	+ to +++
Pumpkin	+	+	+
Rice ("polished") white	—	—	—
Rice, whole grain	+	++	—
Salmon, canned	+	*	*
Shrimp	+	*	*
Spinach, raw	+++	+++	+++
Spinach, cooked	+++	+++	+
Squash, Hubbard	++	*	*
Sugar	—	—	—
Tomato, raw or canned	++	++	+++
Turnip, white	— to +	++	++
Wheat bran	+	+??	—
Wheat flour, white	—	+?	—
Wheat, whole	+	++	—
*Yautía, yellow	++	++	*
*Yautía, white	+	+	*
Yeast	—	+++	—

* D appears to be closely associated with A.

Taken from "Chemistry of Food and Nutrition", by Henry C. Sherman. Third edition.

* NOTE: The *plátano* and *yautías* were tested by D. H. Cook and E. J. Quinn and are not printed in Sherman's text.

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