III

THE "B" FAMILY—VITAMIN B_1, MOTHER OF THE "B" FAMILY

NO animal on earth except man, and on rare occasions the animals which he has made dependent upon him for food, suffer from lack of the vitamins which were formerly grouped together under the letter "B." The vitamin which is now known as B_1, particularly, is so widely distributed in natural foods that only the diabolical ingenuity of man could develop a diet seriously lacking in it. But at least twenty-six hundred years ago man's ingenuity accomplished this very thing. In many parts of the Orient the human animal restricted his agricultural efforts largely to the production of rice, and then developed a method of improving the rice for his consumption by polishing it, i.e., removing the outer coat and germ. In so doing he incidentally removed all the vitamin B_1, which is richly present in the polishings. From that day to this, beri-beri has been one of the principal scourges of mankind in southeastern Asia, and it is no mean distinction to be a principal scourge in that hotbed of human scourges.

In 1879, human beings discovered another process by which to deprive themselves of vitamin B_1—the making of white flour. However, white flour rarely forms nearly so large a part of the diet as is the case with rice in some parts of the world, so the elimination of the wheat germ with the bran was not so serious a matter. Bread may be the staff of life, but fortunately it is not often too exclusively leaned

upon as a support. However, there are exceptions. Beri-beri is not uncommon in northern parts of Labrador and Newfoundland where the menu is made up mostly of white bread, molasses, and salt pork. In 1910 a ship ran ashore up there and lightened its cargo by unloading a large amount of whole wheat flour, with the result that beri-beri disappeared from the region for a year.

In the Japanese navy back in about 1880, one or two out of every five men were sick with this disease. On one ship 195 out of 350 men were down at one time. A brilliant Japanese naval officer concluded that the disease was due to an inadequate diet, and to prove his point he was permitted to experiment with two training ships. Both were sent on a long cruise occupying about nine months. The regulation diet was provided on one of these ships, while a better one was allowed on the other. The ship with the regulation diet had 169 cases of beri-beri and 25 deaths in a crew of 276. On the other ship there were only 14 cases and no deaths.

A few years later, in 1897, Dr. Eijkman, a Dutch scientist in Java, observed in fowls fed on polished rice a disease which he believed was similar to beri-beri, and showed that rice polishings contained something that prevented the disease. He had a survey made of the jails in the Dutch East Indies and the report showed that of every 10,000 prisoners fed on polished rice 3900 had beri-beri, while of those fed on unpolished rice there was only 1 case in 10,000. The fact that the diet was to blame and not an infection, as many believed, was conclusively proved by taking 300 laborers into the jungle where no infections from other human beings could reach them, and where they could be isolated from the unsanitary conditions prevailing in the native villages and on estates. Half of them were put on a diet of polished rice, the other half on less refined food. In three

months beri-beri broke out in the group fed on polished rice while the other group remained healthy. The diets were then reversed, whereupon the group with beri-beri recovered and the group which was formerly healthy became afflicted by it.

About this same time the Americans took over the Philippines and were justifiably shocked at the unsanitary conditions and poor food of the Manila prisons. They killed off the vermin, provided decent sewage disposal, laundered the clothing, and among other improvements in the diet provided clean, white, polished rice instead of the coarse, brown, unhulled rice formerly provided. The result of their well-meant efforts was a severe outbreak of beri-beri that more than nullified all the other benefits. Another example of unexpected disaster from well-meant reform occurred when the League of Nations placed a certain Polynesian island under the mandate of Australia after the World War. The natives, it seems, were prone to indulge in a (to them) delectable alcoholic beverage prepared from yeast. The august and motherly League of Nations felt that so prevalent a state of merriment as existed on the island was unbecoming in a people for whose moral and physical welfare the League was responsible, so it stopped the practice. With the decline of inebriety there was an outbreak of beri-beri, and as in other prohibition experiments the law had to be modified. With the re-introduction of not-too-long-fermented toddies for the mothers the infant death rate fell from 50 to 7 per cent. Still feeling the need of prohibiting something, the government of the island then prohibited white flour and polished rice instead of the cup of cheer, and got better results.

About 1919 suspicions began to arise that vitamin B as then known was in reality a composite of several vitamins,

but it was not until 1926 that the splitting up of the "B family" really began. From that time until the present more and more different offspring from old mother "B" have been shaken loose from the enveloping folds of her skirts. The discovery and identification of these "B" offspring has been a very complicated detective story, to the solution of which many scientists have contributed. Not all the "discoveries" have maintained a place in the esteem of nutritionists, but a number of them have stood the test of time.

Fourteen years after Funk had obtained his anti-beri-beri extract from rice polishings and yeast, vitamin B_1 was obtained in pure form, though in very minute quantities, in the same laboratory in Java where beri-beri was first shown to be due to a deficiency in the diet. Later Dr. R. R. Williams, of the Bell Telephone Laboratories in New York, improved the technique so that larger amounts could be obtained for study, but it still required about two and a half tons of rice polishings to extract one ounce of the pure vitamin. After twenty years of research, in the course of which the molecules of the vitamin were chemically taken to pieces bit by bit to find out what they were made of, and then pieced together again like the parts of a jigsaw puzzle, Dr. Williams finally, in 1936, solved its chemical structure and succeeded in making it synthetically. Now the pure crystalline substance can be obtained in any drugstore at a cent or two per milligram, and 1½ to 2 milligrams per day is all an average man requires. There would be no difficulty in carrying home a year's supply; the equivalent in weight of two aspirin tablets would be more than enough.

The name "thiamin" has been approved for this pure chemical substance. It is water-soluble, and differs from all other vitamins, except the other members of the "B" family, by containing nitrogen. It appears to be one of Nature's

earliest inventions in the evolution of life. It is probably present and necessary in all living things, although the quantity, except where it is especially stored, is usually less than one part in a million. It is necessary for bacteria, fungi, green plants, and all kinds of animals, from amoebae to whales.

Without thiamin, respiration in living organisms is interfered with; the burning of carbohydrates to provide energy cannot go on in a normal manner. The rich deposit of thiamin in the germ of starchy seeds is clearly a provision on the part of Nature to enable the germinating plant to use the starch for energy with which to grow until it can spread its leaves to the sun, whereupon it is able to manufacture more thiamin for its continued use. As Dr. Williams has said, man commits a crime against Nature when he eats the starch from the seed and throws away the mechanism necessary for its utilization. The starch without thiamin is like a safety match without the scratching surface.

Green plants, and many fungi, yeasts, and bacteria are able to manufacture thiamin, but no higher animals are capable of doing so. Green plants make it only in the upper parts, not in their roots, so no root growth is possible without a supply of thiamin either from a supply stored in a seed or from the green portion of a plant. A recent study showed that when root-tips are removed from their parent plants they fail to grow in a plain solution of sugar and mineral salts, but grow well if there is added one part of thiamin in 500,000,000,000 parts of the culture medium. Soaking roots of transplanted plants in a dilute thiamin solution keeps them from wilting, and watering them with it stimulates growth.

In cuttings, the green parts supply enough thiamin to start meager root growth, but much more rapid growth is

stimulated if minute amounts of thiamin are added to the soil or water. This is the reason why cuttings grow better if they are split at the bottom and an oat seed inserted.

Most animals, including man, depend upon outside sources for their thiamin, but some, such as cattle, harbor bacteria in the rumen of the stomach which make it for them in their own alimentary canals. It is for this reason that cow's milk always contains a fair amount of thiamin regardless of the diet, which is not true of human milk. In the Philippines, for instance, mortality from beri-beri is particularly high in breast-fed infants.

The potency of various foods in vitamin B_1 has been measured by various methods of "biological assay." A method which was formerly extensively used was to determine the amounts of a particular food which, if fed daily in addition to a diet entirely lacking in vitamin B_1, would enable rats which had been depleted of the vitamin to make a certain very slight gain in weight each week for two or three weeks. This amount of the food was said to have one Sherman unit of vitamin B_1. In the last few years better methods have been developed. Rats are depleted of the vitamin until they shows signs of polyneuritis. They are then given a test dose of a known quantity of pure thiamin. They recover in a few hours and are then watched to see how many days elapse before the symptoms return. They are then given a certain amount of the food to be tested and the curative effect compared with that produced by thiamin. On the basis of the results obtained smaller or larger doses are given after the rats have relapsed again, until finally the quantity equalling the dose of thiamin is reached. Some assayers prefer to use the rate of the heart beat as a criterion. After two weeks of vitamin B_1 depletion a rat's heart slows from 500 beats per minute to 250, and a dose of thiamin brings it back to nor-

mal for several days. The method is a good one except that it requires an expensive electrocardiograph.

In the last few years other methods of testing for thiamin in blood, urine, and foods have been developed. One method is to find how much of the tested substance is needed to supply enough thiamin to allow a certain mold to grow in a thiamin-free sugar solution. Another is to test its effect on production of alcohol by yeasts. As little as one-millionth of a gram can be detected in this way. There are chemical color tests which are useful in studying body saturation, excretion, etc., but they have not yet been very extensively used for the testing of foods. It is difficult to extract all the thiamin present in foods, and it is doubtful whether even the body accomplishes this during digestion, so the actual vitamin B_1 activity of a food still has to be tested by biological assays on rats, pigeons, or other animals.

The international unit of vitamin B_1 is based on the biological activity of a certain amount of a standard extract of rice polishings adsorbed on Fuller's earth. The unit is equivalent to about 3⅓ micrograms (.0033 mg.) of thiamin. Sometimes "Sherman" units are found on labels; roughly a Sherman unit equals 2 to 3 international units.

Unlike vitamin A, thiamin is stored in the body in rather limited amounts, the largest reserves being in the liver, kidneys, pancreas, and heart. For this reason it is even more important than with most vitamins that the required amount of thiamin be included in each day's food.

Although vitamin B_1 is very widely distributed in Nature, it cannot be said to be *abundant* in any common foods. There is no single food that can be relied upon to supply the major part of a day's requirement. Even the richest sources contain only 20 to 30 parts per million by weight, and most common foods not more than from 0.1 to 4 parts per mil-

lion. It is about 100 times less abundant in foods considered rich in it than is vitamin C in foods in which *it* is rich. On the other hand, very much smaller amounts are required, it is more widely distributed in common foods, and it is not nearly so easily destroyed.

Two to three pounds of food averaging one part of thiamin per million would cover human needs. Such foods supply about 7 units per ounce. The only common foods which average more than 20 units per ounce are various whole grains; liver, heart, and kidneys of various animals; bacon, ham, and sausage among pork products; egg yolk; malted milk powder; green asparagus, string beans, dried beans, lentils, peas, and parsnips among vegetables; and various nuts. Whole wheat bread supplies just about 20 units per ounce, rye bread slightly less. From 7 to 20 units per ounce is afforded by lean meats and fish, whole eggs, milk, and a large variety of vegetables and fruits.

Although the actual content of vitamin B_1 in most fruits is relatively low compared with that of whole grains, nuts, and some vegetables, fresh fruits are nevertheless an important source because of the quantity in which they are eaten and the fact that they are eaten without any cooking or other manipulation which might reduce the vitamins they contain. Yeast is particularly rich in thiamin, but the amount of yeast used in making bread is too small to be of any significance. Wheat germ contains the entire daily requirement of a human being in half an ounce. Prepared bran is only one-fifth as rich in thiamin as is the germ. Oats also contain a relatively large amount.

Polished rice, white flour, and degerminated corn meal and hominy have almost none, but when rice is soaked and parboiled before being milled, the thiamin and phosphorus soak into the starchy part from the hulls and are thereby

saved. This has been a boon to the rice-eating millions in the Orient. Children in Indian institutions still suffer from riboflavine deficiency but they no longer have beri-beri. Pure sugars and starches are entirely lacking in thiamin, and no fats, even butter, contain important amounts of it. Beer, although sometimes advertised as containing vitamin B_1, has a negligible amount.

According to Dr. Sherman of Columbia, one of our leading vitamin investigators, if half the needed food calories are taken as fruits, vegetables, milk, and eggs, and if half of whatever breadstuffs and cereals are used are taken in the whole-grain or "dark" forms, there will almost certainly be provided an ample supply of thiamin—and incidentally other nutritional factors as well. It is doubtful, however, whether this criterion is reached in many American homes.

The solubility of thiamin in water results in considerable loss when fruits or vegetables containing it are soaked or cooked in large amounts of water which is afterwards discarded. Crushed fruits or vegetables lose more than those in which the cells are largely unbroken. Thiamin keeps well in the presence of acids, even when heated, but is destroyed by excessive or prolonged heating in the presence of alkalis like baking soda. It is a pity that so many cooks insist upon adding soda to water in which vegetables are cooked to help preserve their color, for in so doing they not only lose much valuable thiamin, but even larger amounts of vitamin C, which can often be still less afforded. In milk thiamin is particularly stable, possibly because it is accompanied by calcium, which somehow facilitates its utilization. It is not appreciably injured by ordinary boiling.

Tomato juice at its natural acidity, heated for an hour to the boiling point of water, loses only about 10 per cent of its thiamin and a moderate amount of vitamin C, whereas if it

is made slightly alkaline by addition of soda it loses 30 to 40 per cent of its thiamin and nearly all its vitamin C. In ordinary processes of cooking or canning of fruits and vegetables in which the juice is not discarded the thiamin content is fairly well preserved, quite in contrast to the severe destruction of vitamin C which occurs in many such products. The high temperatures required for canning vegetables and meats, however, result in a considerable destruction of their thiamin.

Although the inclusion of too much white bread in the diet only rarely leads to out-and-out beri-beri, it not infrequently leads to less obvious injury, such as loss of appetite, constipation, indigestion, weakness, and loss of weight. This is particularly likely to happen in American homes where white sugar, another refined food, has come to contribute much too large a proportion of the calories in the food. The average per capita consumption of sugar in America has increased nearly tenfold in the last hundred years. Since so much sugar is eaten, providing many calories but no vitamins, it is inevitable that some of the other foods will have to be particularly rich in thiamin, or else so much of them will have to be eaten in addition to the sugar that there will be an excess of calories and a consequent outbreak of bulging waistlines and double chins. The great American diet of steak, potatoes, white bread, and sugar is undoubtedly inadequate in thiamin unless the potato item and accessories are high in proportion to the sugar and bread.

There is still some uncertainty about the exact manner in which thiamin affects the body, and particularly the nerves, but one reason for its indispensability has definitely been pinned down to the fact that without it the metabolism of carbohydrates beyond the pyruvic acid stage (just before its final conversion into CO_2 and water) is interfered with,

and pyruvic acid accumulates, especially in the brain. It is doubtful whether carbohydrate metabolism can go forward in any living cell without thiamin. The most prevalent belief is that thiamin acts as an enzyme to bring about the final oxidation. It certainly enables isolated brain cells to do this. There is also some evidence that it enables the body to build fat out of the pyruvic acid. Just how the failure of the carbohydrate oxidation at the pyruvic acid stage interferes with the nervous system is still to be solved, but the speed of recovery when thiamin is injected under the skull of pigeons sitting with the back of the head touching the back, and turning cartwheels like a decapitated chicken, is little short of magical.

As would be expected, the more calories the body uses the more thiamin is required. This explains why the prodigious use of sweets by Americans, accompanied by extensive use of white bread, but with insufficient vegetables and whole grains, has plagued us with children who won't eat, and who become weak and sickly.

Only severe and continued lack of thiamin results in beriberi. The outstanding symptom of the disease is an extensive degeneration of the nervous system. Both motor and sensory nerves are affected, the former causing paralysis, the latter numbness, itching or prickling sensations, and painful sensitiveness to pressure. The nerve degenerations usually begin in the feet and legs and travel up. In many cases the skin and body cavities fill up with fluid, a condition called dropsy. The lungs, and also the cavity surrounding the heart, fill up with fluid, and the heart itself becomes enlarged and dilated, and slowed in its beat; usually death is caused by its sudden failure. Loss of appetite, constipation, languidness, breathlessness, muscular weakness and sensitiveness, and loss of voice are other characteristic symptoms.

The moaning whine of a baby with beri-beri is characteristic enough to afford a good diagnosis.

The nervous symptoms, dropsy, and severe heart troubles of typical beri-beri are seldom seen in Europe or America, and it was long thought that thiamin deficiency did not occur, but it is now believed that "subclinical" thiamin deficiency is extremely common in American infants and children, and also in women during pregnancy and while nursing. One of the first effects of insufficient thiamin is loss of appetite, probably brought about by an effect on the nerves of the digestive tract. There is less active secretion of digestive juices, less movement of stomach and intestine, slower emptying of the stomach, and greatly impaired absorption of the food that *is* digested. The relative immobility of the intestine is a common cause of gassiness and constipation also, whereas poor absorption may lead to diarrhea; sometimes one condition alternates with the other. People who have suffered from constipation for as long as fifteen years may have regular bowel movements after two months of treatment with thiamin. Children in institutions where the diet was thought to be adequate (300 units a day) have had their appetites improved so much when given 50 per cent extra thiamin that from 17 to 25 per cent more food was consumed. A dog with no interest in food in the morning may, after an injection of thiamin, devour his rations greedily in the evening.

Since most foods which contain thiamin also contain other vitamins, particularly those of the "B" family, it is not surprising that cases of pure thiamin deficiency are rare, and also that a great many people showing evidence of other vitamin deficiencies show some evidence of thiamin deficiency as well. Some degree of thiamin deficiency is undoubtedly a common and possibly an almost universal

accompaniment of pellagra and sprue, and it is undoubtedly involved as a complication in many diseases which affect the alimentary canal or liver. The neuritis and insomnia which frequently develop in dysentery, typhoid, typhus fever, malaria, metal poisoning, alcoholism, etc., is undoubtedly traceable to interference with the proper absorption and utilization of thiamin or other members of the "B" family.

Human requirements of thiamin vary with the weight and the number of calories consumed. For normal adults the amount required has generally been thought to be between 300 and 600 international units per day, or 1 to 2 milligrams, but some recent workers have reckoned it at twice this amount. Infants and growing children, whose calorie intake is relatively high, need more in proportion to their size. In some children it has been found that as high as 3.5 milligrams (1000 units) per day may be retained. There are a number of conditions in adult life also in which extra thiamin is needed, and in which a border-line diet may prove insufficient. People whose metabolism is accelerated by an over-enthusiastic thyroid gland, by pregnancy, or by such febrile diseases as malaria or typhoid, need more than normal individuals. Pregnant women very often develop symptoms of neuritis which indicate lack of sufficient thiamin, probably because of the heavy demands made by the fetus. Often the neuritis is accompanied by pernicious vomiting, low stomach acidity, and other gastro-intestinal troubles. It is difficult in this case to say which is the cart and which is the horse, but the vomiting and dyspepsia on the one hand and low thiamin on the other probably each aggravate the other, to the increasing distress of the patient.

Nursing mothers also require extra thiamin, for if they do not suffer themselves their offspring are liable to—as in the case of the people on the mandated Polynesian island

referred to above. Most mammals appear to be very inefficient in transferring thiamin to their milk; in order to supply their young with an adequate amount they need several times as much as normal or even pregnant animals do. About five or six times as much has to be fed to a rat mother to provide for the needs of her young as when the vitamin is fed directly to the pups.

Another group of individuals who are liable to suffer from deficiency of thiamin are the too-faithful devotees of John Barleycorn. Alcohol has long been blamed for producing a polyneuritis similar to that of beri-beri, but the alcohol is no more *directly* responsible for this than for injuries sustained in an automobile collision resulting from drunken driving.

The alcohol, like sugar, provides an abundance of calories with few vitamins. In addition, topers are notoriously neglectful concerning the non-alcoholic constituents of their diet. The result is a thiamin deficiency brought on by heightened demand and lowered intake. If alcoholics would supplement an otherwise adequate diet with about 0.125 mgs. (40 units) of thiamin per ounce of liquor consumed they would no longer suffer from the neuritis which is so distressing to many of them.

In its relation to carbohydrate metabolism thiamin is intimately related to insulin. In mild cases of diabetes a diet rich in thiamin over a long period will often improve and sometimes cure the condition. On the other hand, a scarcity of thiamin commonly leads to over-development of the islands of tissue in the pancreas which produce insulin. Insulin and thiamin seem to be partners in the business of managing carbohydrates in the body, and insufficiency of one may be made up to a limited extent by an overabundance of the other.

Although there is as yet no evidence that lack of thiamin causes it, the excruciatingly painful facial neuralgia known as "Tic douloureux" can usually be cured, at least temporarily, by injections of thiamin over a period of several months; sometimes liver extract, presumably to supply some other member of the "B" family, is needed as well. Instances are reported of elderly people with this disease being markedly improved after having suffered for over twenty years.

The most recent use found for thiamin is in connection with the treatment of syphilis of the nervous system. When syphilis has reached this stage the only effective drug is tryparsamide; this is dangerous to use because of injurious effects on the optic nerve, often leading to defects in vision or even blindness. Patients treated with thiamin for a few days before being given tryparsamide rarely suffer any injury to the eyes. If this is confirmed on a larger series of cases it may allow the use of tryparsamide in early syphilis and thus prevent neuro-syphilis from developing at all.

One other possible relationship of thiamin is in connection with virus diseases of the nervous system. In recent years nerve diseases such as poliomyelitis and encephalitis have become more prevalent than they used to be. Some people have seen in this a result of the terrific speed of modern life, the continuous round of hurry and worry, of jazz and jitterbugs, of cocktail parties and night-club life. But after all, our ancestors probably put in as much time worrying about witches and superstitions as we do about business and social prestige, and our predecessors who knew nothing of dictation and typewriters probably used up as much nervous energy, albeit more evenly distributed, as those of us who burn up the road getting to an office only to decorate the top of a desk with a pair of number eights while perusing the morning paper. It is at least worthy of some serious

thought whether a chronic mild deficiency of thiamin might not cause a sufficient interference with the normal health of our nervous systems to render them less resistant to virus infections.

When a deficiency of thiamin is discovered it is desirable to administer the vitamin in rather large doses until a normal condition is restored. A daily dose of 10 milligrams (3000 units) is considered conservative for abolishing an accumulated deficit. Even such a huge dose as 90 milligrams seems to be perfectly harmless. The neuritis disappears very rapidly unless the nervous system has been severely injured by a long-continued deficiency. The appetite returns as by magic, and the languor, weakness, and easy exhaustion are soon improved. Large doses of thiamin injected into the blood are a perfect sedative for cases of delirium tremens, and surpass any other treatment in obliterating writhing snakes and pink elephants from the minds of those who have been too long wedded to Ethyl Alcohol.