II

VITAMIN A

BACK at least as far as the time when the children of Israel entered the Promised Land and the Egyptians were building the Temple of Ammon at Karnak, night blindness and tearless, inflamed eyes, the most characteristic symptoms of lack of vitamin A, were known and described. Four centuries before the Star of Bethlehem exerted its guiding power, astute old Aristotle, the Father of Medicine, not only referred to night blindness but mentioned that it could be cured by eating liver. From time immemorial, in periods of famine, war, or isolation from dairy products or green vegetables, men have suffered from vitamin A deficiency. One of the most severe outbreaks in recent years occurred in Denmark during the World War. Food was scarce and prices of necessities as well as luxuries were heading for the stratosphere, but Denmark had an abundance of dairy products which were in such demand by her warring neighbors, and brought such high prices, that the export of butter kept the whole country in bread and clothes. But like the justly celebrated offspring of a shoemaker, the children suffered—they had to subsist on skimmed milk. After a year or two of this, eye troubles, respiratory diseases, skin infections, and stunted growth swept the youth of the land like a plague. When the cause of the trouble was detected, it was promptly remedied, and the children quickly returned to the exuberant state of health which they usually enjoy in a country blessed with milk and butter.

The existence of vitamin A was discovered a quarter of a century ago by two pairs of scientists in the same summer—McCollum and Davis at the University of Wisconsin, and Osborne and Mendel at New Haven. In 1932 England's Professor Drummond concentrated a sticky yellow oil from halibut livers which he thought was nearly pure vitamin A, but it was near the end of 1936 before Dr. Holmes, at Oberlin, finally obtained the pure crystalline substance. It is 50 per cent again as potent as Professor Drummond's thick oil; one gram of it contains three million units. Recently Dr. Hickman of the Eastman Kodak laboratories, by a clever process of "vacuum distillation," has developed a method by which pure vitamin A (and also vitamin D) can be produced at about the cost of a good grade of brandy. He has erected a plant which will produce sixty billion units of vitamin A per week, and hopes to treble that by improved stills now under construction. The vitamin, flavorless and pure, becomes available for mixture with such foods as butter, margarine, or chocolate. The curtain may be falling on the era of crude fish liver oils!

Vitamin A is a fat-soluble substance formed in animal bodies from a chemical cousin called carotene, found in plants. Carotene is deep yellow in color, but it is abundant not only in such yellow-colored vegetables as pimientos, carrots, sweet potatoes, and yellow corn, but also in the green parts of plants. It is only made in sunlight and so is most abundant in thin green leaves; it is about thirty times as abundant in the green outer leaves of a head of lettuce as in the pale heart. It is very abundant in parsley, endive, chard, spinach, and other edible greens, and also in alfalfa and grass. Fruits, with the exception of apricots, are less rich in it, and most grains, starchy tubers, and nuts have negligible amounts.

Vegetable-eating animals obtain their vitamin A in the form of the yellow carotene found in plants, while carnivorous animals usually get it from other animals directly as vitamin A. If taken in as carotene, it is at once converted into vitamin A in the liver, unless there is a large excess. The body has considerable storage capacity for vitamin A, and is generally believed to be able to do without a fresh supply for a long time without suffering, if previously there was an abundance. This may be true so far as severe symptoms are concerned, but recently Dr. Jeghers of the Boston University School of Medicine, after putting himself on several times the necessary daily dose of the vitamin for a number of weeks, cut his intake down to only about one-twentieth of the normal adult requirement. Within a week tests showed lowered ability to see in the dark, and in about a month he had well-developed night blindness. Nevertheless, there is no doubt but that a good excess of vitamin A during the summer months helps to tide people over a long winter season when the supply of the vitamin may be diminished.

There is also evidence that a liberal allowance of this precious substance early in life may have effects, such as well-formed teeth and resistance to infection, which may last throughout life. In other words, what a child eats when he is three years old, possibly even more when he is three months old, has an influence on his health when he is in his "teens." Nature recognizes this; her "survival of the fittest" method of seeing to it that animals do what is best for their kind has provided all young birds and mammals with term health insurance in the form of a fixed vitamin A tax on the parents, deducted at source and deposited in the yolk of eggs and the cream of milk. Even if a hen or a cow has to deplete her own resources of vitamin A to a dangerous extent

to do it, Nature sees to it that she sets aside an adequate amount for the welfare of her young.

This offspring insurance has been a tremendous boon to the human race, for the domestication of cattle and chickens has provided us with a very easy method of getting the carotene of alfalfa, grass, and other greens separated from the roughage to which it is bound, and made available in a concentrated, edible, and palatable form. Milk is undoubtedly the most important single source of vitamin A for most children and many adults, but eggs are a close second. Aside from milk and eggs, and such dairy products as butter and cheese, liver is also important among animal products, since this is where animals store most of their vitamin A. Milk and eggs fluctuate in their vitamin A content according to the food of the animals or birds producing them, but liver is even more variable since its content depends on the excess the animal has for storage. Some fishes store up amazing amounts of both vitamin A and D in their livers, although the amounts of each of these is by no means parallel in different kinds of fish.

Because of its amazing ability to store up vitamin A in its liver, the halibut has come to be one of the most prized denizens of the sea. It is a huge, flat, crooked-eyed, voracious creature living in the depths of cold northern waters. It captures fish and other sea food either by lying in ambush half-buried in the sand, or by active pursuit, stunning codfish and haddock by blows from its powerful tail. The vitamin A which the halibut and other deep-sea fishes so assiduously collect is probably first manufactured as carotene in microscopic marine algae, then converted into vitamin A by the myriads of small crustaceans and other minute drifting animals, and then successively concentrated by small surface fish, larger cod and haddock, and finally by tunas and hali-

but. The millions of units of vitamin A in the liver of a 150-lb. halibut may be the accumulated "take" of twenty-five years of predatory habits.

Fat fish, such as salmon and sardines, provide vitamin A in their flesh as well as in their livers. Oysters, too, are a good source. Although vitamin A is likely to be where the fat is, especially in fishes, there is no correlation between the amount of fat and the amount of stored vitamin A, whether in fish, milk, or human beings. As compared with fish, land animals are very poor collectors of vitamin A. The liver oil of the relatively inefficient cod has from twenty to fifty times as much vitamin A per gram as butter, while that of the halibut has over a thousand times as much.

Vitamin A is not one of the delicate vitamins which are shorn of their power by cooking or preservation. The parent substance, carotene, is even more durable than vitamin A; it is seldom damaged by processes of cooking or canning, although exposure to air at high temperatures has some deteriorating effect upon it. Stored vegetables exposed to warm air, or allowed to ferment, gradually lose some of their carotene potency. For this reason frozen fruits and vegetables, now becoming available by a quick-freezing method which saves them from the injurious effect of large ice crystals in the cells, are likely to have more vitamin A than "fresh" vegetables in a market. Even cooked or canned vegetables may be slightly better.

Vitamin A has two widely different uses in the body. It is a constituent of the light-sensitive pigments in the retina of the eye upon which our vision depends, and it serves as a chemical tool for the normal activities of body cells, particularly epithelial cells.

It has long been known that the rods of the eye are coated with a reddish-purple pigment—called visual purple—that

functions like the silver preparation on a photographic film, being decomposed by even very dim light. This chemical change gives rise to a nerve impulse that causes the sensation of light, and it is on this mechanism that our ability to see in dim light is based. Since the visual purple is a combination of vitamin A and a protein, a deficiency of vitamin A interferes with the production of this substance and consequently with vision at night.

The more visual purple we have, up to a certain maximum, the dimmer the light in which we can see, and the more vitamin A we have, the more rapidly visual purple can be regenerated after it has been decomposed by bright light. People deficient in vitamin A find difficulty in driving a car at night, are unable to see faint stars, and sit in other people's laps when getting seated in a darkened theatre.

Blindness following exposure to the glare of headlights at night is due to decomposition of visual purple by the light, and its duration depends on the speed with which the pigment can be replaced. In a normal individual this takes only a few seconds, but in one suffering from lack of vitamin A it takes much longer, and a fast-traveling car may have to be driven hundreds of feet in complete blindness. Many a wrecked car and broken body would be spared if parents as well as children would eat more spinach, or put more butter on their bread.

When the vitamin A deficiency is mild there is often no consciousness of reduced night sight, but there are delicate tests by which even very slight abnormality can be detected. The use of these tests has demonstrated an amazing and unsuspected prevalence of insufficient vitamin A even in typical American communities. A recent investigation of a series of children in Iowa showed defective ability to see in the dark in 26 per cent in rural schools, 53 per cent in a county seat

of 2000 population, and 56, 63, and 79 per cent, respectively, in the upper, middle, and lower economic levels in a city of 150,000. Of seventy-eight of the defective children who were given three teaspoonfuls of cod-liver oil daily (to supply vitamin A) only three failed to improve, and the majority were normal in from four days to a month. Even more striking was a recent survey by Dr. Jeghers of 162 students in the Boston University School of Medicine. Fifty-five were below normal in ability to see in the dark. The following table of comparison with normal students is enlightening:

	Students with normal night vision	*Students with impaired night vision*
Ate at home	74%	42%
Ate in restaurants	16%	32%
Ate in quarters	10%	26%
Those eating in quarters averaged weekly	$4.20	$2.80
More than one full meal per day	100%	40%
Average duration of colds	5.5 days	7.4 days
Total number of days of illness	47	136

The students with inadequate vitamin A were more frequently those eating away from home, spending too little on their food, and subsisting on doughnuts and coffee for breakfast, and sandwiches, sodas, etc., for lunch. About half of the defective students were conscious of their night blindness—they sat in other people's laps when getting seated in a darkened theatre, and were unable to drive a car at night except on lighted streets. A third of them also complained of dryness of the skin, and three of dry eyes. Several

noticed that their annoyance from dry skins disappeared after a summer at home with mother's cooking.

Another recent investigation was made in an Ohio yarn factory, where the employees complained of eyestrain; they couldn't read after a day's work, their eyes smarted and burned, and they made too many errors in color matching. After three capsules a day of carotene in oil their mistakes decreased by 75 per cent, they had far more eye comfort, and in many cases their general health improved.

Until very recently the mechanism of daylight vision—with which the cones of the eyes are concerned—was unknown, although many similarities between the behavior of rods and cones suggested a similar mechanism for both. In 1937 it was shown that the cones also possess a light-sensitive pigment, though it is very dilute, and that this pigment—called visual violet—is also dependent upon vitamin A. Vitamin A is therefore an important factor in day as well as night vision.

The other evidences of vitamin A deficiency, which fortunately are not striking when the deficiency is slight, are due to obscure effects on the normal activity of body cells, particularly the epithelial cells. Rats which are fed on a diet that has everything except vitamin A stop growing as soon as their stored vitamin is used up, lose vigor, become susceptible to infections, especially of the respiratory system, skin, and intestine, develop dry, sore eyes which finally become blind, and are prone to develop kidney stones. Recently early-developing injury to nerve cells and fibers has been observed in various animals, followed by such effects as paralysis and lack of muscular control. Female rats have their sexual cycle disturbed, and males, ceasing to produce sperms, become sterile. The teeth during growth have their enamel improperly developed. There is every reason to be-

lieve that all of these symptoms would develop in human beings as well if no vitamin A were supplied, but with more moderate deficiencies the injuries are often so indefinite as to escape realization. Vitamin A is used up in considerably larger amounts by growing children than by adults, and it is rapidly depleted in septic infections such as pneumonia, sinusitis, appendicitis, etc.

This epithelium constitutes the first line of defence against invasion of germs. It forms a stratified, resistant layer of horny cells in the skin; ciliated cells for sweeping dust and germs out of the lungs; a delicate, transparent film over the eyes; mucous cells to moisten the alimentary canal; secreting cells in all sorts of glands; sperm-producing cells in the testes; enamel-depositing cells in the developing teeth; etc. In the absence of vitamin A all the epithelial cells except those of stomach, intestine, and kidneys fail to become specialized for their particular parts, and tend to form flat, horny cells like those of the skin, which is often very inappropriate and undesirable. Even in the alimentary canal the mucus-producing goblet cells become greatly reduced in number, and there is evidence that these cells are instrumental in protecting the intestine against parasites. In the eyes the delicate conjunctival membrane which covers the exposed surface is normally kept moist and clean by a film of oil and a constant flow of tears; without vitamin A it becomes dry and dirty, the lids swell and become scabby, and pus flows instead of tears. When the deficiency in vitamin A is severe, the dry, inflamed condition of the eye leads to infections which may cause blindness. There are thousands of cases of blindness of this type in India and Africa.

In the respiratory system defective epithelium allows germs to get a foothold, and disease follows—colds, sinus troubles, bronchitis, middle ear infections, etc. When peo-

ple who have been getting along on too little vitamin A are given an adequate amount they often notice a marked difference in the number and duration of colds. In the alimentary canal insufficient mucus secretion leads to ulcers, erosion, poor absorption, and diarrhea. A poor grade of epithelium in the genital organs leads to delayed menstruation, miscarriages, or failure to produce sperms. An extra amount of vitamin A during the last month of pregnancy reduces the chance of mild infections following childbirth. Pregnancy and breast feeding drain away reserves at a rapid rate, and this is also true of the changes at puberty; rats on poor vitamin A diets are very likely to get lung diseases just as they are maturing, and it may be more than coincidence that human beings, too, are especially likely to "go into a decline" with consumption soon after puberty.

When the teeth are forming, some epithelium which sinks below the surface of the gum assumes the specialized function of taking up minerals and depositing them as a veneer of enamel over the underlying dentine; without vitamin A these cells fail to become specialized as stone masons, and the enamel does not form normally; even the underlying dentine is abnormal because the dentine cells seem to be organized and directed by the enamel organ covering them. Vitamin A deficiency during the period of tooth formation probably does even more than lack of vitamins C and D to plague us with soft, easily decayed teeth. Kidney stones, too, are associated with vitamin A deficiency: in a recent investigation in Philadelphia twenty-four of twenty-five kidney stone patients showed evidence of inadequate vitamin A by their night blindness, although most of them failed to improve when treated with vitamin A. It was believed their deficiency was due to an abnormal inability to assimilate or make use of the vitamin. It is claimed that a diet rich in

vitamin A sometimes causes kidney stones to redissolve. Kidney and bladder stones, as well as blindness, are very common in Northern India where milk and butter are scarce, and the climate too austere for growing much besides grain.

When the only evidence of vitamin A deficiency is a slight lowering of ability to see in the dark, an improvement of the diet to bring the vitamin intake up to normal is all that is required, but when noticeable symptoms have developed it is best to take large daily doses until a normal condition is reached, which may require several weeks. There has been considerable difference of opinion as to what human requirements of vitamin A are, but recent use of the "biophotometer" to measure normality of sight in dim light indicates that a daily intake of 4000 to 5000 international units (2.4 to 3 milligrams) is close to the minimum for normal adults, whereas growing children require relatively larger doses. Professor Mary Rose, of Columbia Teachers College, suggests 280 units per 100 calories in the diet for growing children, which would make it range from about 3000 units in a child under a year old to over 8000 at puberty. For pregnant and nursing women a daily intake of 8700 units has been recommended by the League of Nations Committee on Nutrition. There are some who think that even this is not generous enough, yet an investigation in a Massachusetts hospital out-patient department showed that less than one in ten of such women were getting over 7000 units per day. In England a few years ago a significant decrease in sickness among pregnant women was observed following the administration of cod-liver oil, and it was believed that the vitamin A was the effective ingredient in the oil, the vitamin D having very little to do with it. It would be excellent insurance if all expectant or nursing mothers would take daily a teaspoonful of cod-liver oil, or better still a few drops of hali-

but-liver oil, to provide the extra vitamin A they need. This will supply about 3000 units, a quart of milk will provide 1500 to 2000 more, and the rest will come mainly from other dairy products, eggs, and green or yellow vegetables.

It should be kept in mind by vegetarians that carotene is not as completely absorbed from the intestine as is the vitamin A of dairy products, eggs, liver, or fish oils. A recent investigation in India showed that from 35 to 55 per cent of the carotene of the food passed out of the body in the feces, whereas every bit of the vitamin A was utilized. In cases of jaundice, where bile is missing from the intestine, carotene, like fatty acids, fails to pass the border patrol and is wasted (also true of vitamin K and probably E), whereas the converted vitamin A is admitted on its own passport. Mineral oils interfere with absorption of carotene much more than of vitamin A by dissolving it and carrying it out of the body. Vitamin A is said to be injured by contact with iron salts or rancid fats.

There is no danger of overdosage with carotene or vitamin A. Doses of 100,000 units a day are sometimes given in cases of extreme deficiency. If a great excess of carotene is absorbed it is deposited in the subcutaneous fat and gives the skin a golden glow, but it does no harm. In a milk-producing animal excess carotene is also excreted in the milk, giving it a yellow color, but the yellow color of cream and eggs is no indication of its vitamin A value, for there are other causes of deep color, especially in eggs, and even very pale cream or eggs may be rich in colorless vitamin A.