Vitamin B_6 in Human Nutrition

Among the vitamins of the B complex, B_6 has remained in relative obscurity because, during most of the twenty-year period since its discovery, its place in human nutrition remained unknown. Tentative reports of its value in the treatment of nausea of pregnancy and x-ray sickness were discounted as psychogenic, and the importance of evidence based on animal research tended to be minimized as inapplicable to man.

During the past two years, clinical evidence has accumulated to show beyond any reasonable doubt that B_6, a stepchild among vitamins, has a very real place in human nutrition. Credit for this discovery belongs to L. Emmett Holt and co-workers,[1] who observed convulsions in one mentally retarded young infant and anemia in an older child—both restricted to a vitamin B_6-deficient diet. Both of these manifestations (which yielded quickly to administration of pyridoxine) had been observed previously in young animals.

Holt's isolated report might have failed to achieve general recognition and might have been dismissed as a fortuitious result of brain damage associated with mental deficiency, had it not been for a chain of events involving a popular infant food, liquid S-M-A.®

Reports of convulsive seizures in a very small percentage (about 3 to 5 per thousand) of very young infants on an unsupplemented diet of liquid S-M-A® appeared at first sporadically and in a limited area; then, as attention was directed to these cases, additional reports began to come from widely separated communities.

Despite the report of Holt which, by hindsight, should have explained easily the course of events, the finger of suspicion was not directed at vitamin B_6 deficiency until very recently.

False clues and factors, which should have been, at best, of merely contributory significance, were strewn all about. First reports centered about a drought area in Texas, where mineral-surcharged artesian well water, used as a diluent for liquid S-M-A®, seemed a logical clue; in a nearby community where the use of bottled water was the rule, there were no instances of convulsions. But when the suspected water was used to dilute powdered S-M-A®, convulsions never occurred.

Another scapegoat for the convulsions in some infants was the change which had been made in the character of the fat in S-M-A®, in order to achieve the lower intestinal pH characteristic of a human milk diet. It had been shown by Barbero *et al.*[2] that the composition of the fat was a major factor in predisposing the intestinal flora in favor of the acidophilic *Lactobacillus bifidus*—hence the incorporation of palm oil in S-M-A® fat.

A change in the fat of S-M-A®—then convulsions in infants. Suspicion, no matter how unfounded it subsequently proved to be, was too devastating to be ignored; so quickly, all the new-fat S-M-A® was recalled and the old-fat formula reinstated. But there never had been any trouble with powdered S-M-A®, and it had the same fat!

Extensive laboratory studies revealed no trace of toxic material to account for the convulsions in some infants. Good scientific sense demanded that a factor be found in liquid S-M-A® that did not occur in the powder that had the same ingredients except for water. The only difference was in the processing: the liquid product required a higher temperature of autoclaving. Heat processing of foods containing protein and sugar is a known cause of destruction of amino acids, vitamins, and of complex chemical changes involved in Maillard's browning reaction. What, then, was destroyed? If Holt's observations on one patient were correct, and the previous observations on animals were applicable to man, thermal destruction of vitamin B_6 might be the real culprit.

A microbiological study[3] of the vitamin B_6 content of various milk products was immediately arranged for, but without awaiting the outcome of this work, pyridoxine hydrochloride was immediately added to liquid S-M-A®.

This study of milk preparations disclosed or confirmed these facts:

1. Milk from any source contains three

kinds of vitamin B_6: pyridoxal, pyridoxamine, and pyridoxine. Among these the first two are very easily destroyed by heat, while pyridoxine is relatively heat-stable.

2. Because S-M-A®, as manufactured, has a lower content of whey-constituents and a protein level close to that of human milk, its pre-autoclaving vitamin B_6 content is rather low—a point that never had seemed to matter, since no human need for this vitamin had been recognized. The high autoclaving temperature necessary for liquid S-M-A® further reduced the natural vitamin B_6 content, most of which was heat-labile.

3. When pyridoxine, the heat-stable form of vitamin B_6 was added to liquid S-M-A® before autoclaving, as is now the practice, thermal destruction proved minimal, and even after terminal autoclaving the food has an adequate vitamin B_6 content.

Since this action was taken, not a single case of convulsions in infants connected with liquid S-M-A® containing B_6 has been reported.

The most dramatic and convincing evidence that the convulsive syndrome under discussion was wholly due to pyridoxine deficiency was supplied by Dr. David B. Coursin of Lancaster, Pa., who, for a two and one-half hour period, recorded the brain waves of a young infant who had developed convulsions on an exclusive unsupplemented liquid S-M-A® diet and had gone into status epilepticus.

During the recording of the electroencephalogram, Dr. Coursin injected saline solution, which produced no change either in the EEG or in the patient's clinical condition. Finally, he injected 100 mg. pyridoxine intramuscularly, whereupon the pathologic brain wave pattern virtually disappeared within three minutes, while the infant patient's convulsions ceased and peaceful sleep ensued. Since then the patient has continued entirely well on an unsupplemented liquid S-M-A® diet for a period of two and one-half months, with an entirely normal mental and physical development.

Besides this striking report,[4] confirmatory observations have been received as private communications from more than twelve other pediatricians who volunteered to continue infants on liquid S-M-A® after convulsions developed, prescribing only small occasional injections of pyridoxine hydrochloride. Under this regimen, all the infants recovered promptly and enjoyed a perfectly normal development.

Even before such deficiencies were recognized, interesting evidence that a limited vitamin B_6 intake, sufficient to satisfy the needs of most infants, may produce striking deficiency symptoms in a few, had been supplied by Hunt, Stokes, McCrory and Stroud,[5] who aptly described this puzzling metabolic defect in one such infant as "B_6-dependency." In the case reported by them, a young infant who had been in a serious convulsive state for several weeks after birth responded dramatically to supplementary pyridoxine by mouth or by injection.

Recently Vilter[6] and co-workers reported observations in adults receiving a vitamin B_6 antimetabolite (desoxypyridoxine). Foremost among the clinical signs of B_6 deficiency seen in 34 of 50 patients participating in this experiment were (*a*) anorexia, nausea, listlessness; (*b*) seborrhea sicca-like dermatitis; (*c*) cheilosis and conjunctivitis; (*d*) glossitis; (*e*) pellagra-like dermatitis; and (*f*) polyneuritis. In addition, mild anemia and other changes in the blood picture were noted in some cases.

These observations, viewed in relation to one another, compellingly suggest these conclusions:

1. Vitamin B_6 is essential in human nutrition.

2. This need is amply satisfied by the diet usually avaliable to adults, children, and all but the youngest of infants.

3. The convulsive seizures that were seen in a few young infants on a marginal vitamin B_6 intake disappeared completely in all cases following administration of pyridoxine, either in the food or by injection. No permanent damage was found in treated cases.

Inevitably and regrettably, this vital new nutritional knowledge was acquired at the expense of some human suffering. This has been the fate of every major discovery in nutrition. —PAUL GYÖRGY, M.D.

REFERENCES

1. Snyderman, S. E., Holt, L. E., Jr., Carretero, R., and Jacobs, K.: Pyridoxine deficiency in the human infant. *Fed. Proc.* 9: 371, 1950; J. Clin. Nutrition 1: 200, 1953.
2. Barbero, G. J., Runge, G., Fischer, D., Crawford, M. N., Torres, F. E., and György, P.: Investigations on the bacterial flora, pH, and sugar content in the intestinal tract of infants. *J. Pediat.* 40: 152, 1952.
3. Hassinen, J. B., Durbin, G. T., and Bernhart, F. W.: The vitamin B_6 content of milk preparations. In press.
4. Coursin, D. B.: Convulsive seizures in infants with pyridoxine-deficient diet. *J. A. M. A.* 154: 406, 1954.
5. Hunt, A. D., Stokes, J., McCrory, W., and Stroud, H.: *Pediatrics.* In press.
6. Vilter, R. W., Mueller, J. F., Glazer, H. S., Jarrold, T., Abraham, J., Thompson, C., and Hawkins, V. R.: The effect of vitamin B_6 deficiency induced by desoxypyridoxine in human beings. *J. Lab. & Clin. Med.* 42: 335, 1953.

Changing Minds and Diets

"Intelligence plays relatively little part in what we eat; hence, an intellectual approach has limited value, although it is the easiest to use. . . . One explains, one repeats for emphasis, one augments by demonstration, and, for good measure, one adds a written list for future reference. In this approach, the specialist tells the person what he should do and why. So far so good, but the 'teaching' needs to be preceded with the preparation of the patient for learning and must be followed by much more.

The patient must want to change his pattern of eating; he must want to change enough to offset the force of his habit of years. He must want to change the food pattern because he wants something more than he wants his customary food. He may want to get back to work, to feel like himself again, or to feel safe. He may accept change because there is something he wants to avoid. He may want to avoid pain, or weakness, or diabetic coma. What he is willing to do about his food when he is on his own will relate to his comprehension of the relation of food to what he wants to avoid or gain."

—Grace White. *Journal of the American Dietetic Association* 30: 25, 1954.