Metabolism and Function V I T A M I N B$_1$ in RUMINANT: A Review

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Abstract: Thiamin (vitamin B$_1$) was the first vitamin to be discovered. Under most circumstances, there is few chance of thiamin deficiency for mono gastric animals, including humans, when diets contain ample quantities of whole cereal grains or starchy roots. However, many thiamin antagonists in the food supply, and sensitivity of the vitamin to processing, can lead to deficiency. Thiamin deficiency in humans has been a problem mostly in Asian countries, where highly milled rice is consumed, therefore laminating the thiamin-rich bran fraction of the grain. For years, it was accepted that ruminants didn't require vitamin B supplementation thus of enough rumen micro flora synthesis. Intensification of ruminant feeding, involving high-concentrate diets, and management systems by increased levels of production have resulted in nervous disorders which are responsive to thiamin supplementation.

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Introduction

Vitamins are defined as a group of complex organic compounds current in nominal amounts in natural foodstuffs that are essential to normal mal metabolism and lack of which in the diet causes deficiency diseases. Vitamins consist of a mixed group of chemical compounds and are not related to each other as are proteins, carbohydrates, and fats. Their classification together depends not on chemical characteristics but on function. Vitamins are differentiated from the trace elements, also present in the diet in small quantities, by their organic nature.

Vitamins are required in trace amounts in the diet for health, growth, and reproduction. Omission of a single vitamin from the diet of a species that requires it will produce deficiency signs and symptoms. Many of the vitamins function as coenzyme others have no such role, but perform certain essential functions. Some vitamins deviate from the preceding definition in that they don't always need to be constituents of food. Certain substances that are considered to be vitamins are synthesized by intestinal tract bacteria in quantities that are often adequate for body needs. However, an obvious distinction is made between vitamins and substances that are synthesized in tissues of the body. Ascorbic acid, for example, can be synthesized by most species of animals, except when they are young or under stress conditions. Likewise, in most species, niacin can be synthesized from the amino acid tryptophan and vitamin D from action of ultraviolet light on precursor compounds in the skin. Thus, under certain conditions and for specific species, vitamin C, niacin, and vitamin D would not always fit the classic definition of a vitamin.

Classically, vitamins have been divided into two groups based on their solubility's in fat solvents or in water. Thus, fat-soluble vitamins include A, D, E, and K, while vitamins of the B-complex and C are classified water soluble. Fat-soluble vitamins are found in foodstuffs in association with lipids. The fat-soluble vitamins are absorbed along with dietary fats, apparently by mechanisms similar to those involved in fat absorption. Conditions favorable to fat absorption, such as adequate bile flow and good micelle formation, also favor absorption of the fat-soluble vitamins (Scott et al., 1982).

Chemical structure

Thiamin consists of a molecule of pyrimidine and a molecule of thiazole linked by a methylene bridge (Fig.1); it contains both nitrogen and sulfur atoms. Thiamin is isolated in pure form as the white thiamin hydrochloride. The vitamin has a characteristic sulfurous odor and slightly bitter taste. Thiamin is very soluble in water, sparingly so in alcohol, and insoluble in fat solvents. It is very sensitive to alkali, in which the thiazole ring opens at room temperature when pH is above 7. In a dry state, thiamin is stable at 100^{o}C for several hours, but moisture greatly accelerates destruction, and

thus, it is much less stable to heat in fresh than in dry foods. Under ordinary conditions, thiamin hydrochloride is more hygroscopic (takes up moisture) than the mono nitrate form. However, both products should be kept in sealed containers. Autoclaving destroys thiamin, an observation that played an important role in the discovery that what was originally considered to be a single vitamin was actually a member of the vitamin B complex (Maynard et al., 1979).

Substances with an anti-thiamin activity are fairly common in nature and include structurally similar antagonists as well as structure altering antagonists and thiamin-degrading enzymes (thiaminases). The synthetic compounds pyrithiamine, oxy thiamine, and amprolium are structurally similar antagonists, and their mode of action is competitive inhibition with biologically inactive compounds, thus interfering with thiamin at different points in metabolism. Synthetic thiamin antagonists are often used in studies of the pharmacodynamics of thiamin (Barclay and Gibson, 1982).

Heat-stable thiamin antagonists occur in a number of plants (e.g., ferns and tea); these include polyphenols, which oxidize the thiazole ring to yield the nonabsorbable thiamin disulfide. Tall fescue (*Festuca arundinacea* Schreb.) toxicosis resembles diseases caused by enhanced rumen thiaminase activity. Thiamin supplementation has been found to reduce tall fescue toxicosis (Lauriault et al., 1990).

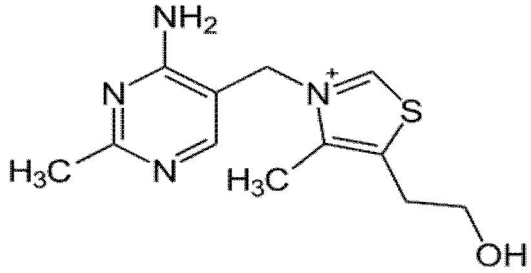

Fig1: structure Vitamin B_1, from www.Wikipedia.com.

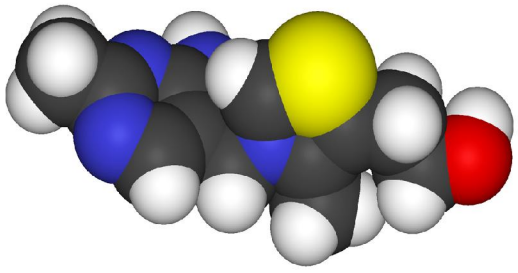

Fig 2: structure multi aspect of Vitamin B_1, from www.Wikipedia.com.

Sulfur has been shown to be antagonistic to thiamin enzymes. The sulfite ion has been shown to cleave thiamin from enzymes at the methylene bridge between the pyrimidine and thiazole rings and analytically will mimic thiaminase. Sulfate increases thiamin-destroying activity in the rumen contents, and the destructive mechanism involves thermola- bile factor(s); however, the ruminal synthesis of thiamin is not affected by sulfate (Olkowski et al., 1993).

Thiaminase activity destroys thiamin activity by altering the structure of the vitamin. The disease Chastek paralysis in foxes and other carnivores fed certain types of raw fish results from a thiaminase that splits the thiamin molecule into two components, thus inactivating it. Two types of thiaminase enzymes have been described. Thiaminase II simply cleaves the vitamin at the methylene bridge between the thiazole and pyrimidine rings. Thiaminase I substitutes a nitrogen-containing ring for the thiazole ring. This leads to less thiamin, but it also gives rise to thiamin analogs composed of the pyrimidine ring of the original thiamin, and another ring from the "co-substrate." This created thiamin analog inhibits one or more thiamin-requiring reactions necessary for energy metabolism in the central nervous system (CNS).

Since thiaminase is heat labile, the problem can be avoided in fish, for example, by cooking the fish at 83^{O}C for at least 5 minutes. Many kinds of fish contain thiaminase, and thiamin deficiency has been reported in penguins, seals, and dolphins fed primarily fish diets in zoos. Thiaminase is found mainly in herrings, sprats, stints, and various carp species—a total of some 50 species, most of which live in fresh water. Wild aquatic animals apparently do not develop thiamin deficiency even though they eat a diet primarily of fish, because fish must undergo some putrefaction to release the enzyme.

Metabolism

Digestion, Absorption and Transfer

Hiamin is readily digested and released from natural sources. A precondition for normal absorption of thiamin is sufficient production of stomach hydrochloric acid. Phosphoric acid esters of thiamin are split in the intestine. Free thiamin is soluble in water and easily absorbed. Absorption occurs in the small intestine, particularly in the jejunum. In most species, absorption is negligible in the distal portion of the small intestine, and in the stomach and large intestines. Therefore, thiamin synthesized by gut micro flora in the cecum or large intestine is largely unavailable to the animal except by coprophagy. The horse, however, can absorb thiamin from the cecum.

Ruminants can also absorb free thiamin from the rumen, but the rumen wall is not permeable for bound thiamin or for thiamin contained in rumen microorganisms. The mechanism of thiamin absorption isn't yet fully understood, but apparently both active transport and simple diffusion are involved.

At low concentrations there is an active sodium-dependent transport against the electro-chemical potential, whereas at high concentrations it diffuses passively through the intestinal wall. Absorption from the rumen is also believed to be an active mechanism. Absorbed thiamin is transported via the portal vein to the liver with a carrier plasma protein, thiamin-binding protein (Brown, 1990).

This binding protein is hormonally regulated and is associated with thiamin transport into and out of the cell. In blood, 90% of total thiamin is in the cellular fraction (predominantly erythrocytes), while the plasma contains largely free unesterified thiamin.

Storage and Excretion

In animal tissues, thiamin occurs mostly as phosphate esters. Although thiamin is readily absorbed and transported to cells throughout the body, it is not stored to any great extent. Thiamin content in individual organs varies considerably, with the vitamin preferentially retained in organs with high metabolic activity. During deficiency, thiamin is retained in largest quantities in important organs such as the heart, brain, liver, and kidneys. The principal storage organs are the liver and kidney; however, approximately one-half of total thiamin is present in muscle. Thiamin is one of the most poorly stored vitamins. Mammals can exhaust their body stores within 1 to 2 weeks (Ensminger et al., 1983).

Since thiamin is not stored in large amounts, it is relatively easy to develop severe deficiency in a short time, even in adult animals. Thiamin intakes in excess of current needs are rapidly excreted. This means that the body needs a regular supply and that unneeded intakes are wasted. The pig is somewhat of an exception, however—for some unknown reason its tissues contain several times as much

It has been shown that decarboxylation of the three branched-chain α-ketoacids derived from the deamination of leucine, isoleucine, and va-line are also oxidatively decarboxylated by a multienzyme complex analogous to those for pyruvic and α-ketoglutaric acids, but more specific for these branched-chain α-ketoacids (Gubler, 1991).

TPP is a coenzyme in the transketolase reaction that is part of the direction oxidative pathway (pentose phosphate cycle) of glucose metabolism that occurs not in mitochondria but in thiamin as other species studied. Thus it has a store that can meet body needs on a thiamin-deficient diet for as long as 2 months (Heinemann et al., 1946).

Functions

Thiamin in all cells functions principally as the coenzyme cocar-boxylase or TPP. Thiamin monophosphate is completely inactive, and any coenzyme activity previously attributed to the triphosphate undoubtedly results from partial conversion to di phosphate by hydrolysis of the terminal phosphate ester bond by thiamin triphosphatase (Gubler, 1991).

The citric acid cycle is responsible for production of energy in the body. In this cycle, breakdown products of carbohydrates, fats, and proteins are brought together for further breakdown and for synthesis. The vitamins riboflavin, niacin, and pantothenic acid, as well as thiamin, play roles in the cycle. Thiamin is the coenzyme for all enzymatic decarboxylations of α-keto acids. Therefore it functions in the oxidative decarboxylation of pyruvate to acetate, which in turn is combined with coenzyme A for entrance into the tri-carboxylic cycle.

In mammals, thiamin is essential in two oxidative decarboxylation reactions in the citric acid cycle that take place in cell mitochondria and one reaction in the cytoplasm. These are essential reactions for utilization of carbohydrates to provide energy. Decarboxylation in the citric acid cycle removes carbon dioxide, and the substrate is converted into the compound having the next lower number of carbon atoms. In the mitochondria, reactions pyruvate dehydrogenase forms acetyl CoA from pyruvate and α-ketoglutarate dehydrogenase to convert α-ketog- lutarate to succinyl CoA as follows:

$$\text{Pyruvate} \blacklozenge \text{acetyl-CoA} + CO_2 \quad (1)$$

$$\alpha\text{-Ketoglutaric acid} \blacklozenge \text{succinyl-CoA} + CO_2 \quad (2)$$

the cell cytoplasm in liver, brain, adrenal cortex, and kidney, but not skeletal muscle. Trans- ketolase catalyzes transfer of C_2 fragments; hence with ribulose 5-phosphate as donor and ribose 5-phosphate as acceptor, sedoheptulose 7-Phosphate and triose phosphate are formed. This is the only mechanism known for synthesis of ribose, which is needed for nucleotide formation of RNA and DNA synthesis and results in formation of nicotinamide adenine dinucleotide phosphate (NADP), which is essential for reducing intermediates from

carbohydrate metabolism to form fatty acids. It can also supply intermediate sugars for glycolysis.

Thiamin has a vital role in nerve function, although the mechanism of action is unclear. It has been postulated that thiamin, probably as TPP, plays an essential role in nerve transmission, apart from its enzymatic role in the Krebs cycle and the pentose pathway. When nerves are stimulated, the levels of TPP and TTP decrease, and TMP and free thiamin are released into the surrounding medium. This is believed to involve sodium and potassium transport at the membrane.

Fatty acids and cholesterol are the major constituents of cell membranes, and effects on their synthesis would affect membrane integrity and function. Thiamin deficiency in cultured glial cells impairs their ability to synthesize fatty acids and cholesterol. The defect is related to reduce formation of key lipogenic enzymes. These changes could be the basis of degenerative changes seen in glial cells in early thiamin deficiency.

Stimulation of nerves by either electrical or chemical means has been found to result in the release of thiamin that is associated with the dephosphorylation of its higher phosphate esters. The antagonist pyrithiamine can displace thiamin from nervous tissue and change the electrical activity of the tissue. Possible mechanisms of action of thiamin in nervous tissue include the following:

(1) Thiamin is involved in the synthesis of acetylcholine, which transmits neural impulses; (2) thiamin participates in the passive transport of sodium of excitable membranes, which is important for the transmission of impulses at the membrane of ganglionic cells; and (3) the reduction in the activity of transketolase in the pentose phosphate pathway that follows thiamin deficiency reduces the synthesis of fatty acids and the metabolism of energy in the nervous system.

Thiamin has been shown to have a role in insulin biosynthesis. Isolated pancreatic islets from thiamin-deficient rats secreted less insulin than those from controls.

Effect of deficiency

The classic diseases, beriberi in humans and polyneuritis in birds, represent a late stage of thiamin deficiency resulting from peripheral neuritis, perhaps caused by accumulation of intermediates of carbohydrate metabolism. Comparing signs of thiamin deficiency in various species, one sees that disorders affecting the CNS are the same in all species. This is explained by the fact that in all animals, the brain covers its energy requirement chiefly by the degradation of glucose and is therefore dependent on biochemical reactions in which thiamin plays a key role.

In addition to neurological disorders, the other main group of dis- orders involves cardiovascular damage. Clinical signs associated with heart function are slowing of heartbeat, enlargement of the heart, and edema. Les specific clinical signs include gastrointestinal problems, muscle weakness, easy fatigue, hyperirritability, and lack of appetite. Of all nutrients, thiamin deficiency has the most marked effect on appetite. Animals consuming a low-thiamin diet soon show severe anorexia, lose all interest in food, and will not resume eating unless given thiamin. If the deficiency is severe, thiamin must be force-fed or injected to induce animals to resume eating. Animals developing thiamin deficiency most readily are chickens and rabbits are less readily depleted, probably because of endogenous thiamin production.

Ruminants

Young animals that do not have a fully developed rumen can be thiamin deficient, as shown in experiments with calves and lambs (Mc-Donald, 1982).

Clinical signs include apparent weakness that is usually first exhibited by poor leg coordination, especially of the forelimbs, and by inability to rise and stand. The head is frequently retracted along the shoulder, and the heart may develop arrhythmia. Specific signs are usually accompanied by anorexia and severe diarrhea, followed by dehydration and death. Signs in the calves can be either acute or chronic. In one study, acutely affected calves were anorectic, had severe diarrhea, and died within 24 hours. These signs appeared after 2 to 4 weeks on a low-thiamin diet (Johnson et al., 1948).

The term PEM refers to a laminar softening or degeneration of brain gray matter. However, it is commonly used to describe the CNS condition in ruminants. The condition affects mainly calves and young cattle between 4 months and 2 years old, and lambs, young sheep, and goats between 2 and 7 months old. The incidence of PEM is reported to be between 1 and 20%, and mortality may reach 100%. Clinical signs in mild cases include dullness, blindness, muscle tremors and opisthotonos. The condition ischaracterized by circling, head pressing, and convulsions, and in severe cases, the animal collapses within 12 to 72 hours after onset of the disease. Because of the circling, the condition is sometimes called “circling disease.” The ears drop, and in the final stages, the limbs and head are extended. General twitching of the musculature of the ears and eyelids, waving of the head and neck, and grinding of the teeth with groaning sometimes

occur. Without treatment, death usually comes within a few days. The main lesions in these animals are necrotic areas in both cerebral hemispheres.

PEM may run a short, acute course or may occur in a milder form and run a more protracted course. The condition, particularly in its mild form, probably is often not diagnosed and may occur more frequently than is recognized. Clinical signs of CNS disorders associated with PEM are more readily recognized than nonspecific signs such as scouring, reduced growth, and anorexia. However, these signs are exhibited at later stages of thiamin deficiency (Rammell and Hill, 1986).

Animal on thiamin-deficient diets may not show clinical signs of a CNS disorder for 3 to 5 weeks or longer, although depressed blood thiamin levels and other clinical signs may be observed. Without treatment, mortality is about 50% of animals with the mild form and possibly up to 100% in animals with acute PEM. The incidence and death rates are higher in young animals from 2 to 5 months of age than for animals older than 1 year High-sulfur diets are associated with thiamin deficiency and PEM.

Steers with the highest rumen fluid sulfide concentrations coincided with the onset of clinical signs of PEM. Several cases of PEM occurred when gypsum had been used as a feed intake limiter. It would appear that the sulfate ion of gyp- sum, during its conversion to sulfide, must pass through sulfite, which may destroy thiamin. The sulfite ion apparently will cleave thiamin at the methylene bridge, mimicking thiaminase (McAllister et al., 1992).

In lamb, PEM was induced by administration of a sulfide solution; neurological clinical signs included stupor, visual impairment, and seizures (McAllister et al., 1992).

Feedlot cattle that received 0.72% sulfate had 50% less gains than controls, and 3 of 20 head developed PEM. Supplementation of sheep feed diets high in sulfur (0.63%) had clinical sign of PEM that were prevented with supplemental thiamin (243 ppm) (Olkowski et al., 1992).

However, thiamin did not totally prevent development of microscopic brain lesions, which are characteristic of PEM. In sheep, high sulfur intake was shown to have a detrimental effect on *In vitro* polymorphonuclear leukocyte function. This can mean that ruminants in areas where large quantities of sulfur are taken in with water and feed have compromised immune function due to lower copper and thiamin status and hence are at risk of increased susceptibility to infections (Olkowski et al., 1990).

Field studies (Olkowski et al., 1991) found an inverse correlation between water sulfate content and blood thiamin in beef cattle. Cattle receiving water with less than 200 ppm of sulfate had higher blood thiamin than cattle receiving water with over 1,000 ppm of sulfate. Feedlot nutritionists have reported cases of PEM when high percentages of wet-milled corn by-products were fed. Sulfuric acid is used to steep corn in the wet-milling process; much of the sulfur then remains with by-product.

Livestock grazing endophyte-infected (*Acremonium coenophiatum*) tall fescue develop tall fescue toxicosis. Clinical signs of fescue toxicity include reduced feed intake and growth, elevated body temperature, and ergot-like clinical signs with necrosis in the extremities. The cattle exhibited typical signs of summer fescue toxicosis compared to cattle grazing endophyte-free fescue. Following grazing, the cattle were fed corn: corn silage diets with and without supplemental thiamin. Dietary supplementation with 0.5 g of thiamin during the feedlot phase improved the daily weight gain by 0.19 kg/day.

Tall fescue toxicosis resembles conditions caused by enhanced rumen thiaminase activity that may treat with thiamin (Edwin et al., 1968).

Responses to supplemental thiamin were found to be greater when cattle grazing endophyte infected tall fescue were exposed to heat stress (Lauriault et al., 1990).

Results suggest that oral thiamin supplementation may alleviate tall fescue toxicosis of beef cattle during warm weather. A contrary earlier report (Fontenot et al., 1988) found that feeding thiamin to cattle grazing mod- erately endophyte-infected fescue had no beneficial effect.

Zintzen (1974) concluded that PEM can be definitely established if the following four situations exist:

1. Case history: Animals have been maintained on high-energy feeds rich in carbohydrates, and other animals on the same farm have, from time to time, died after exhibiting CNS disorders.
2. Biochemical evidence: Blood pyruvate has steeply increased, and the activity of erythrocyte-transketolase has been reduced.
3. Diagnosis and therapy: Animals thought to have PEM react promptly to treatment with thiamin provided they are treated in the early stages of the disease.
4. Pathological changes: Necropsy shows typical pathological anatomical changes (bilateral cortical necrosis) in the brain.

Seasonal trends have been associated with PEM, which may be due to increased metabolic demands of gestation, lactation, and growth. Additionally, feeding high-concentrate diets may induce PEM.

In goats in Bikaner, India, PEM was prevalent throughout the year, with the highest incidence in late winter. It was suggested that scarcity of grazing may have led the animals to consume plants containing substances with thiaminase activity.

Polioencephalomalacia generally occurs in feedlot cattle, frequently about 3 weeks after a ration change. Research suggests that PEM is associated with lactic acid acidosis, with both conditions related to adaptation to grain diets.

Thiamin in the rumen is decreased by a reduction in rumen pH; a low ruminant pH is characteristic of cattle fed high-concentrate diets. Although little information is available on the direct addition of thiamin to finishing cattle diets. In a third trial, thiamin administered alone gave an intermediate response to calves immediately after weaning.

PEM has caused significant economic losses in tropical countries, not only in feedlots where high-grain diets are provided, but also where high levels of molasses are fed. When molasses is provided (ad libitum) together with rations containing little crude fiber, a disease referred to as "molasses toxicity" or "molasses drunkenness" occurs. Clinical signs of this condition closely resemble PEM, and studies completed in Cuba have suggested that thiamin treatment, together with additional roughage, may be an effective cure (Losada et al., 1971).

A number of experiments have shown that PEM is caused by naturally occurring thiamin antagonists, in connection with reduced thiamin synthesis or destruction of the vitamin. Several researchers have reported that most field cases of PEM result from progressive thiamin deficiency, likely a result of gut and ruminal bacterial thiaminases. Clinical reports of PEM have shown that under high-concentrate feeding systems of beef cattle and lambs, thiaminase may become active in the rumen and cause thiamin deficiency in animals with functional rumens. These thiaminases may be produced by microorganisms in contaminated feeds. Thiaminase I has been shown to increase in the feces when dairy cows were switched from a low- to high-concentrate diet. Amprolium's mode of action as a coccidiostat is apparently through inhibition of thiamin phosphorylation. High levels of amprolium could produce the physical signs and the histological lesions of PEM (Loew and Dunlop, 1972).

Both *Clostridium sporogenes* and *Bacillus thiaminolyticus* have been isolated from the rumen of PEM cases. Both organisms produce thiaminase type I. Thiaminases are found in certain plant species and are produced by microorganisms believed to be responsible for PEM. This has been a special problem in Australia, where PEM occurs under pasture conditions, apparently being derived from some of the fern species.

Humans

The disease occurs in a wet form, characterized by edema and cardiovascular symptoms, and a dry form, characterized by peripheral neuritis, paralysis, and muscular atrophy. However, the forms merge, making it hard to differentiate the two. The chronic form may last for years; cardiac symptoms may appear suddenly and result in death within a short time. It is generally believed that the more serious the nervous lesions, the greater the muscular pain and weakness and the less likely the development of acute beriberi. The heart is saved from extreme insufficiency by forcing the patient into complete rest at an early stage in the attack.

General symptoms of beriberi include anorexia, heart enlargement, tachycardia lassitude and muscle weak-ness, paresthesia, loss of knee and ankle reflex with subsequent foot and wrist drop, ataxia due to muscle weakness, and dyspnea on exertion. The "squat test" illustrates the neurological damage, as beriberi patients are unable to rise from a squatting position (Gubler, 1991).

The signs and symptoms vary depending on age, individual, diet, duration and severity of the deficiency, and abruptness of onset. Peripheral neuropathy is a symmetrical impairment, with loss of sensory, motor, and reflex function affecting the distal segments of limbs more severely than the proximal ones, and with less cardiac involvement. Disturbances of the higher nervous centers, nystagmus, and ophthalmoplegia are frequent. In advanced stages, patients exhibit general muscular atrophy, ataxia, mental confusion, and defective short-term memory. The sequence of symptoms is variable, but beriberi often begins with numbness in feet, heaviness of legs, prickly sensations, and itching. Muscles become tender, and squeezing the calf of the leg causes pain. Cardiac symptoms develop at some stage and are characterized by palpitation, epigastric pain, coldness of extremities, and enlargement of the heart. Later symptoms and clinical signs include edema of ankles, puffiness of face, digestive disturbances, anorexia, nausea, and vomiting.

Infantile beriberi, common in the Orient, is an acute form of the disease. It is probably an important cause of the high infant mortality in South Asia. Nursing mothers, who provide milk

deficient in thiamin, may or may not show mild signs of deficiency. The condition usually occurs in the first few months of life and begins with anorexia, regurgitation, abdominal distention, and colicky pain. Oliguria is followed by edema, and there is dyspnea, with a peculiar cry or grunt thought to be caused by edema of the vocal cords. Later, cardiovascular signs and congestive failure increase and nervous signs appear, with muscular twitching, coma, and death. Cardiac failure is often the cause of death. Phase may last only a few hours, and the whole course of the condition only a day or two.

In countries where large amounts of fish are eaten raw, human thiamin deficiency may occur. Elsewhere, poverty, alcoholism, food faddism, or poorly prepared food may result in inadequate thiamin ingestion. A variety of malabsorptive disorders can jeopardize nutritional status with respect to thiamin. Acute polyneuropathy developed one patient after jejunoileal bypass surgery and thiamin blood status was found more depleted in patients with Crohn's ailment.

Studies have suggested that some degree of thiamin deficiency is widespread in the elderly. This may result mostly from generally poor appetite and eating habits or low income. However, it has been demonstrated that old rats require more thiamin per gram of food eaten than young rats, and transport of thiamin across the intestine is significantly lower in older than younger rats (Marks, 1975).

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I was appreciating those parents because they are helping always.

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