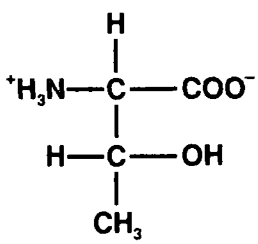
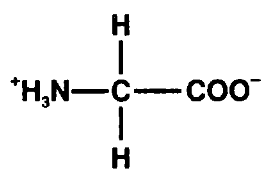
SECTION SIX

Threonine Amino Acids

THREONINE
The Immunity Booster



GLYCINE
The Wound Healer



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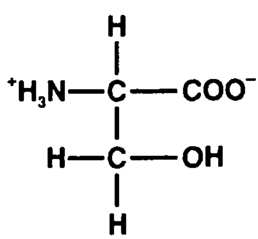

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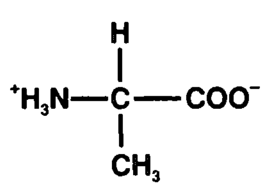

CHAPTER THIRTEEN

Threonine: The Immunity Booster

Threonine is a little-known essential amino acid that is a necessary building block for all protein, especially for tooth enamel, collagen, and elastin. It promotes the growth of the thymus, a small gland that regulates many of the hormones and cells vital to immune defense. Even a moderate reduction in dietary intake of threonine can produce a profound depression in immune response.

FUNCTION

Threonine is the precursor of glycine and serine, two other amino acids in the threonine group. It is present in the heart, central nervous system, and skeletal muscle. Threonine has been identified as being one of the essential agents that protect against mental instability, irritability, and "difficult" personalities.

Intravenous administration of threonine increases glycine and threonine concentration in the spinal cord and brain. This method of increasing glycine in the brain is of importance because glycine, which acts as a sedative in the brain, may not enter the brain well. Large doses of glycine, 30 g for example, are necessary to produce glycine's sedative effect.

Just as the neurotransmitters acetylcholine, serotonin, catecholamines, and histamine have been demonstrated to be dependent upon the availability of dietary precursors, it appears that neurotransmitter concentrations of glycine may be dependent on dietary sources of threonine as well as on glycine. Glycine can be made by the body from glucose and other energy sources, but it has generally been assumed that dietary intake of glycine is relevant to its concentration and synthesis. Yet a deficiency of threonine dehydratase, the enzyme that breaks down threonine, has been thought to be a cause of hyperglycinemia (elevated glycine levels). This suggests that threonine is converted to glycine and glycine to threonine and that these amino acids are often therapeutically interchangeable. The conversion rate may, however, be slow.

Threonine can help to stabilize blood sugar since it can be converted into glucose in the liver by gluconeogenesis (formation of glucose from noncarbohydrate substances such as amino acids). Low levels of threonine can result in hypoglycemic conditions, especially if accompanied by low levels of serine or glycine.

Threonine has been shown to be useful in indigestion and to improve intestinal absorption. It helps to metabolize fat and acts as a lipotropic in controlling fat buildup in the liver.

Threonine also seems to benefit people who have been burned, wounded, or undergone surgery. In such trauma, threonine appears in higher than normal levels in urine. This suggests that threonine is released from the tissue following trauma to aid in the healing process. Threonine also appears to help in the formation of cyanocobalamin (vitamin B_{12}), a substance essential for the metabolism of the sulfur amino acids.

METABOLISM

Threonine, like all amino acids, requires adequate amounts of pyridoxine (vitamin B_6) to be metabolized properly. It is broken down primarily by the enzyme threonine dehydratase. The activity of this enzyme decreases with age.

In addition to serving as a precursor of glycine and serine, threonine can be degraded into propionic acid and methylmalonic acid as can methionine and valine.

REQUIREMENTS

Threonine is an essential amino acid, and so cannot be manufactured in the body from other amino acids. It is therefore critical that sufficient amounts be included in the diet. Like the needs for most essential amino acids, requirements for threonine appear to decrease with age. Infants four to six months old require 68 g a day, while children aged four to twelve need only 28 g, and adults seem to require just 8 g per day.

In animal studies, seventeen experimental kittens on threonine-deficient diets developed neurological dysfunction and lameness; the symptoms were resolved with dietary supplements of threonine.

The relatively low requirement estimated for adults has been challenged by several studies that suggest that adult requirements for threonine and several other essential amino acids are underestimated. More realistic approximations suggest an average adult male needs 15 mg/kg of threonine per day.

Aging individuals require more threonine supplementation under stress. In our plasma amino acid survey of 100 patients, we found no significant difference between baseline threonine levels in different age groups, however, there is no question that threonine requirements increase during stress.

15x70=1.05 gm

FOOD SOURCES

Good levels of threonine can be found in most animal proteins, cottage cheese, and wheat germ. There is substantially less threonine content in grains; therefore, vegetarians are more likely than others to have deficiencies if the diet is not supplemented. Other potential nonmeat sources of this amino acid include beans, brewer's yeast, nuts, seeds, soy, and whey.

TABLE 13.1. THREONINE LEVELS IN FOOD

FOOD	AMOUNT	CONTENT (GRAMS)
Avocado	1	0.13
Cheese	1 ounce	0.25
Chicken	1 pound	1.00
Chocolate	1 cup	0.36
Cottage cheese	1 cup	1.37
Duck	1 pound	1.35
Egg	1	0.30
Granola	1 cup	0.40
Luncheon meat	1 pound	2.40
Oatmeal	1 cup	0.43
Pork	1 pound	3.40
Ricotta	1 cup	1.27
Sausage meat	1 pound	1.15
Turkey	1 pound	1.50
Wheat germ	1 cup	1.35
Whole milk	1 cup	0.36
Wild game	1 pound	4.00
Yogurt	1 cup	0.32

FORM AND ABSORPTION

Dietary and supplemental sources of threonine occur in the L- form. To utilize threonine optimally, pyridoxine (vitamin B_6), magnesium, and niacin are needed. Valine, isoleucine, and leucine are also suggested to assure that maximum effects can be achieved.

CLINICAL USES

The amino acids in the threonine group have simple chemical structures. Glycine is the cornerstone of each amino acid in this group. It works as an amino sugar and allows all the amino acids in this group to function as sugar exchangers. Therapeutically, they function as brain stimulants and immune controllers.

Depression

At our clinic, we have found 1 g of L-threonine in the morning and in the evening to be a useful adjunct therapy in agitated depression and manic depression. Threonine levels normalize on this therapy.

Of our first 100 depressed patients administered plasma amino acid profiles, fifteen showed low threonine levels. All fifteen patients had either primary or secondary diagnosis of severe depression. This group also included two patients with epilepsy, one with phenylketonuria, two with chronic schizophrenia, one with folliculitis (a bacterial infection of the hair follicle), and one with multiple myeloma (a cancer of the bone marrow). Several of these depressed patients responded to threonine therapy.

Of the first 128 depressed patients we tested, three had elevated threonine levels. Two patients were taking tryptophan, cysteine, and other amino acids, and one was taking the asthma medication theophylline (Theo-Dur).

Immune Stimulation

Interest in threonine has been aroused by studies conducted on the effect of dietary threonine and lysine on the immune response. Rats fed diets containing wheat gluten, supplemented with threonine and lysine, were found to significantly increase thymus weight as well as increase immunoglobulin response. The results showed that the influence of threonine in the system was real and not related to an increase of body weight. Other studies suggest that a high number of accepted allografts, transplants that are successful because of immunosuppression, occur in threonine-supplemented rats. Overall, most studies find that threonine is an immunostimulant.

A moderate reduction of dietary threonine produced a profound depression of the immune response or antibody production (a protein created by the

Threonine Helps Patient Gain Control of Depression

A sixty-two-year-old man with severe psychotic depression, peptic ulcer, spastic colon, and high blood pressure came to us desperate for relief. The patient did not improve on antidepressants. He had extremely low threonine levels—43 percent of normal. One 500-mg capsule of L-threonine in the morning and in the evening led to gradual control of his depression within one month.

immune system capable of destroying or neutralizing a foreign organism or toxin) against tumor growth in mice. It is not surprising that glycine also has immunostimulant properties, since threonine is metabolized into glycine.

Lotan and colleagues suggest that the effects of threonine relate to a specific requirement by the thymus for this amino acid.

We have found threonine given orally to be of some value in patients who are extremely sensitive to wheat gluten. Doses of 2 to 4 g of threonine per day allow these patients to safely add some wheat to their diets.

Muscle Spasticity

Using threonine supplements to increase brain glycine levels stimulated pilot studies using threonine supplementation in human muscle spasticity. Barbeau and colleagues used 1 g of L-threonine in patients suffering from multiple sclerosis (MS) and familial spastic paraplegia (a group of disorders characterized by progressive stiffness or spasticity of the legs with varying degrees of weakness). The result showed an overall improvement in spasticity and mobility of lower limbs by 25 percent.

In another study, 500 mg of L-threonine was administered two times a day for twelve months to six patients with genetic spasticity syndrome, followed by a four-month observation period. All six patients showed partial improvement of spasticity, with an increase in intensity of knee jerks but a decrease in intensity of muscle spasms. Measurement of upper limb showed 29 percent improvement and a 42 percent improvement in lower limb measurements; the range of overall improvement was 19 to 35 percent. No toxic, clinical, or biochemical changes were reported.

These results warrant a controlled trial in well-defined, preferably genetic cases of spasticity.

Plasma Levels in Clinical Syndromes

Alcohol ingestion causes histidine levels to decline significantly and threonine levels to increase substantially in the plasma of normal adults. We frequently find deficient levels of threonine in epileptic and depressed patients, occasionally in association with low plasma glycine levels.

Threonine levels increase in animals treated with sedative anticonvulsants. The lowest threonine levels we found were in a twenty-eight-year-old patient with epilepsy who had been on the anticonvulsant phenytoin (Dilantin) and phenobarbital (Solfoton) for ten years.

THREONINE LOADING

We asked volunteers to take 5 g of L-threonine after they fasted. At two hours, threonine levels were five times normal, and four times normal at four hours.

Generally, peak absorption is at two hours. Levels of the amino acids valine, isoleucine, leucine, and tryptophan decreased, and glutamine increased. Other biological parameters such as chem screen, polyamines, and trace metals did not change.

High dose therapy of 5 g of L-threonine daily most likely does not alter the plasma amino acid levels until more than two weeks after initiation of therapy. We gave one patient daily oral doses of 5 g for two weeks and did not observe any change in plasma amino acids except in threonine, which increased from low to normal to high levels.

SUPPLEMENTATION

At present, there is no known therapeutic use for threonine in the brain. However, it may be beneficial in providing biochemical support for people with genetic spasticity disorders and multiple sclerosis.

Deficiency Symptoms

There are no known signs or symptoms of threonine deficiency.

Availability

Free-form L-threonine is available in 500 mg capsules.

Therapeutic Daily Amount

Suggested doses for therapeutic purposes range from 300 to 1,200 mg a day. To utilize threonine optimally, pyridoxine (vitamin B_6), niacin (vitamin B_3), and magnesium are needed. Valine, isoleucine, and leucine are also recommended to assure maximum effect.

Maximum Safe Level

Not established.

Side Effects and Contraindications

None known.

THREONINE: A SUMMARY

Threonine is an essential amino acid in humans. It is abundant in human plasma, particularly in newborns. Severe deficiency of threonine causes neurologic dysfunction and lameness in experimental animals.

At our clinic, we frequently find low levels of threonine and glycine in depressed patients. These patients respond to 1 g of threonine in the morning and in the evening. Plasma levels of threonine are a useful way to monitor treatment.

Threonine is an immunostimulant that promotes the growth of thymus gland. It also can probably promote cell immune defense function. This amino acid has been useful in the treatment of genetic spasticity disorders and multiple sclerosis at a dose of 1 g daily.

Threonine may increase glycine levels. It is highly concentrated in meat products, cottage cheese, and wheat germ. Additional important uses of threonine as a useful therapeutic agent are likely to be found as studies continue.

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