

# The Nutritional Relationships of Vitamin A

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## Introduction

Vitamin A, the first fat-soluble vitamin to be recognized, has been described as one of the most versatile vitamins due to its many roles in body functions. The most well-defined function of vitamin A is its role in vision. It is also involved in maintenance and integrity of the mucous membranes, skin, remodeling, and growth of bones. Other roles include maintaining the stability of cell membranes and nerve sheaths, synthesis of adrenal cortical hormones (corticosterone), and regulation of thyroxin output. Vitamin A is also involved in the manufacture of red blood cells and assists the immune reaction. More recently researchers have suspected that vitamin A is involved in cellular differentiation and gene expression. Over the past 10 years vitamin A has been investigated for the prevention and treatment of various types of cancers.<sup>1 2 3</sup>

## Vitamin A Requirements

The terminology for the measurement of vitamin A is presently in transition. This is due to the various forms of the pre-vitamin, which are converted into the active form (retinol) at different efficiencies. Therefore the term retinol equivalents (R.E.) is beginning to replace international units (I.U.). RE is the amount of retinol a vitamin A compound will yield following conversion by the body. Recommended dietary allowances for infants and children are 420-700 RE, males 1,000 RE, females 800 RE. During pregnancy and lactation, the RDA is increased 200 and 400 RE respectively. Larger doses of short duration are required when deficiency symptoms exist.

## Hypovitaminosis A

The most recognized early sign of vitamin A deficiency is night blindness (im-

paired night vision), xerophthalmia, and Bitot's spots. Roughness of the skin occurs due to hyperkeratosis of the hair follicles. During development, a deficiency of vitamin A leads to abnormalities in dentine formation and bone growth.

Causes of vitamin A deficiency include inadequate intake, impaired absorption or storage, and poor conversion of carotene to active vitamin A. Poor absorption and/or storage is associated with excessive alcohol intake, celiac disease, cystic fibrosis of the pancreas, ulcerative colitis, biliary obstruction, and cirrhosis of the liver.<sup>4</sup>

## Hypervitaminosis A

Toxicity of vitamin A occurs with protracted high doses. Acute toxicity has been observed following the consumption of polar bear liver, which contains 20,000 I.U. per gram.<sup>5</sup>

Symptoms of vitamin A toxicity include joint pain, decalcification, and fragility of bone. Increased intracranial pressure produces pseudo brain tumor symptoms. Red blood cells lose hemoglobin, and bleeding can occur easily. Nervous system symptoms include irritability, restlessness, fatigue, anorexia, and muscle weakness. Rashes may develop on the skin, causing dryness and peeling along with hair loss. The lips may also become scaly. The spleen and liver enlarge and jaundice may develop.<sup>6</sup> Symptoms of toxicity subside with reduced intake of the vitamin.

## Vitamins Synergistic to Vitamin A

As with minerals, rarely does a vitamin deficiency develop singularly. Synergistic co-factors should also be taken into consideration when determining vitamin A requirements and during therapy.

Vitamin E is considered synergistic to vitamin A due to its antioxidant activity, which results in a sparing effect upon vitamin A.<sup>7</sup> Vitamin E also aids in stabilization of cell membranes. Loss of vitamin A from liver stores is accelerated in the

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presence of vitamin E deficiency as a result of increased fragility of lysosomal membranes.<sup>8</sup>

Vitamin C is also thought to act as an antioxidant for hepatic vitamin A stores. Animal studies have shown that vitamin A has an influence on the hepatic synthesis of ascorbic acid.<sup>9</sup> Any nutrient having antioxidant activity can be considered synergistic to vitamin A.

Because of its synergistic effect upon the mineral zinc, vitamin B<sub>6</sub> can be considered synergistic to vitamin A.<sup>10</sup> Zinc is, of course, involved in the regulation of vitamin A.<sup>11</sup>

The B complex in general has been associated with vitamin A activity. Besides B<sub>6</sub>, vitamin B<sub>1</sub>, B<sub>2</sub>, B<sub>3</sub>, and B<sub>5</sub> have been specifically described as vitamin A synergists.<sup>12</sup>

#### **Vitamins Antagonistic to Vitamin A**

Figure 1 indicates the vitamins that are considered to be antagonistic to vitamin A. Vitamin A may also be considered antagonistic to these vitamins.

Vitamins D and A are often considered synergists and, in a supplement form, are frequently given in combination. However, vitamin A can be given to reduce the toxic effects of hypervitaminosis D.<sup>13</sup> In general the fat soluble vitamins compete for absorption and transport; therefore, the entire fat soluble family can be considered antagonistic.<sup>14</sup> The different effects on bone metabolism also indicate vitamin A and D antagonism. Vitamin D increases the absorption and retention of calcium, while excess vitamin A causes bone resorption and decalcification.

Being oil soluble, vitamin E may compete with vitamin A for absorption. Vitamin A is known to suppress vitamin E levels in immunopoietic tissue.<sup>15</sup>

The antagonistic effects are also indicated by the opposite effects of vitamins A and E on prostaglandin E<sub>1</sub> and E<sub>2</sub> (PGE<sub>1</sub> PGE<sub>2</sub>) synthesis. Vitamin E suppresses PGE<sub>2</sub><sup>16</sup> and enhances PGE<sub>1</sub> synthesis, while vitamin A enhances PGE<sub>2</sub> synthesis. High levels of vitamin E intake may also interfere with beta carotene absorption.<sup>17</sup>

Due to its copper lowering effect, vitamin C may contribute to the oxidation of vitamin A by increasing tissue iron ac-

cumulation.

Other vitamins having a potential to antagonize vitamin A include B<sub>1</sub>, B<sub>12</sub>, B<sub>6</sub>, and K. Their mechanisms of action are not completely understood but probably adversely affect vitamin A when stores or intakes are extremely low. They can also increase vitamin A utilization.

#### **Minerals Synergistic to Vitamin A**

The mineral zinc is intimately associated with vitamin A. Adequate amounts are required for the mobilization of vitamin A from the liver. In several experiments involving animal and human studies, vitamin A deficiency symptoms did not respond to vitamin A supplementation alone when a zinc deficiency co-existed. However symptoms of vitamin A deficiency, such as impaired night vision, improved only after zinc supplementation. Zinc is involved in maintaining the plasma retinal binding protein (RBP), a specific transporter for vitamin A.<sup>18</sup>

Iron deficiency anemia is associated with low vitamin A status as well as reduced hemoglobin levels.<sup>19</sup> Vitamin A apparently facilitates the mobilization of stored iron for incorporation into erythrocytes.<sup>20</sup>

Selenium is involved in antioxidant activity and therefore can be considered synergistic to vitamin A. Both vitamin A and selenium have similar effects upon inhibiting carcinogenesis.<sup>21</sup>

Other minerals synergistic to vitamin A include magnesium, manganese, potassium, and phosphorus. Like vitamin A, these minerals are closely related to thyroid function.<sup>22</sup>

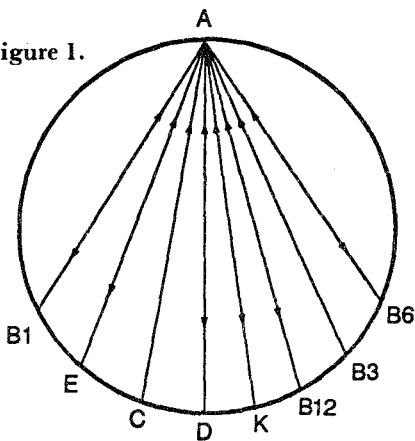
#### **Minerals Antagonistic to Vitamin A**

Figure 2 shows the minerals that are considered antagonistic to vitamin A. Vitamin A may also be mutually antagonistic to these elements.

Excessive tissue iron accumulation may increase vitamin A requirements due to destruction by peroxidation. Excess iron accumulation can occur due to a severe copper deficiency.<sup>23</sup>

Even though selenium is an antioxidant, under certain circumstances and in large amounts, it can act as a pro-oxidant, resulting in adverse effects on the fat

Figure 1.



soluble vitamins.<sup>24</sup>

Iodine in the form of  $T_4$ , although synergistic to vitamin A, is antagonistic as well.<sup>25</sup>

The minerals copper, calcium, and sodium can have an indirect antagonistic effect upon vitamin A due to their interrelationship with the thyroid gland.<sup>26 27</sup>

Any factor that antagonizes the mineral zinc can be a potential antagonist to vitamin A, e.g., cadmium and mercury.

### Endocrine Relationship to Vitamin A

As with minerals, vitamins are also affected by endocrine activity. Hormone levels can directly affect vitamin A status and requirements.

### Thyroid and Vitamin A

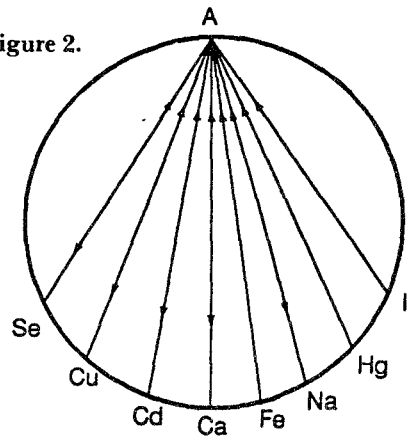
The conversion of carotene to vitamin A is influenced by thyroxine. Studies show that thyroidectomy or suppression of the thyroid produces hypercarotenemia and reduced retinol levels in the liver.<sup>28 29</sup> It has been speculated that vitamin A deficiency is associated with hypothyroidism. Studies reveal that low vitamin A levels are associated with goiter formation.<sup>30</sup>

Overactivity of the parathyroid due to its suppressing effect upon the thyroid and its relationship with vitamin D may also increase vitamin A requirements.<sup>31</sup>

### Estrogen and Vitamin A

Tissue estrogen sensitivity is increased in the presence of vitamin A deficiency.<sup>32</sup> The concentrations of RBP are lowest prior to the preovulatory peak in estradiol levels. According to the study reported by Keyvani, et al, females are affected by goiter more than males due to the fact that

Figure 2.



females have lower vitamin A levels.

### Adrenal Hormones and Vitamin A

The adrenocortical hormones increase the mobilization of vitamin A from the liver. This effect has also been reported in the treatment of rheumatic children with cortisone.<sup>33</sup> Adequate adrenal function is also necessary for the mobilization of vitamin A stores. It is possible that adrenal and thyroid insufficiency contributes to signs of vitamin A deficiency or increased requirements due to an inability to mobilize it from storage.

### Protein

Adequate protein is necessary for the mobilization of vitamin A from the liver to the blood stream. Vitamin A deficiency is associated with protein malnutrition. Normal serum vitamin A levels can be restored when protein is added to the diet, providing there are adequate liver reserves of the vitamin. However, if liver reserves of vitamin A are depleted, dietary protein may precipitate an acute vitamin A deficiency.<sup>34</sup>

### Assessment of Vitamin A Status

Over 90% of the vitamin A reserves are in the liver; therefore, serum levels do not truly reflect vitamin A status. The serum levels however do reflect a deficiency when liver reserves are depleted and an excess when liver stores are over saturated.<sup>35</sup>

### Conclusion

As with other nutrients, requirements for vitamin A should be assessed in conjunction with its co-factors. Nutritional

therapeutics involving vitamin A may be greatly enhanced when the synergists and antagonists are taken into consideration.

Since vitamin A is closely related to the thyroid gland, it can be speculated that subclinical deficiencies are related to hypothyroid conditions. Some of the more common symptoms associated with hypothyroidism that may respond to vitamin A include hyperlipidemia, atherosclerosis, adult onset diabetes, fatigue, depression, cold sensitivity, changes in skin and hair texture, and anemia.

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