Clinical Nutrition Service, Warren Grant Magnuson Clinical Center • Office of Dietary Supplements • National Institutes of Health

Vitamin A and Carotenoids

As a consumer, you need information you can trust to help you make thoughtful decisions about eating a healthful diet and using vitamin and mineral supplements. Registered dietitians at the Warren Grant Magnuson Clinical Center, the clinical research hospital at the National Institutes of Health (NIH) in Bethesda, MD, developed this series of Fact Sheets in conjunction with the Office of Dietary Supplements in the Office of the Director of NIH to provide responsible information about the role of vitamins and minerals in health and disease and to help guide your decisions on the use of vitamin and mineral supplements. Each fact sheet in this series received extensive scientific review by recognized experts from the academic and research communities. The information is not intended to be a substitute for professional medical advice. It is important that you seek the advice of a physician about any medical condition or symptom. It is also important to seek the advice of a physician, registered dietitian, pharmacist, or other qualified health care professional about the appropriateness of taking dietary supplements and their potential interactions with medications.

Vitamin A: What is it?

Vitamin A is a family of fat-soluble vitamins. Retinol is one of the most active, or usable, forms of vitamin A, and is found in animal foods such as liver and eggs and in some fortified food products. Retinol is often called preformed vitamin A. It can be converted to retinal and retinoic acid, other active forms of the vitamin A family (1-4). Some plant foods contain darkly colored pigments called provitamin A carotenoids that can be converted to vitamin A. In the U.S., approximately 26% and 34% of vitamin A consumed by men and women is provided by provitamin A carotenoids (1).

Beta-carotene is a provitamin A carotenoid that is more efficiently converted to retinol than other carotenoids (1-4). For example, alpha-carotene and b-cryptoxanthin are also converted to vitamin A, but only half as efficiently as beta-carotene (1). Lycopene, lutein, and zeaxanthin are other carotenoids commonly found in food. They are not sources of vitamin A but may have other health promoting properties. The Institute of Medicine (IOM) encourages consumption of carotenoid-rich fruits and vegetables for their health-promoting benefits.

Vitamin A plays an important role in vision, bone growth, reproduction, cell division and cell differentiation, which is the process by which a cell decides what it is going to become (1, 5-8). It helps maintain the surface linings of the eyes and the respiratory, urinary, and intestinal tracts (9). When those linings break down, bacteria can enter the body and cause infection (9). Vitamin A also helps maintain the integrity of skin and mucous membranes that function as a barrier to bacteria and viruses (10-12).

Vitamin A helps regulate the immune system (2, 5, 13). The immune system helps prevent or fight off infections by making white blood cells that destroy harmful bacteria and viruses. Vitamin A may help lymphocytes, a type of white blood cell that fights infections, function more effectively.

Some carotenoids, in addition to serving as a source of vitamin A, have been shown to function as antioxidants in laboratory tests. However, this role has not been consistently demonstrated in humans (1). Antioxidants protect cells from free radicals, which are potentially damaging byproducts of your oxygen metabolism that may contribute to the development of some chronic diseases (3, 14-16).

What foods provide vitamin A?

Preformed vitamin A is found in animal foods such as whole eggs, whole milk and liver. Most fat free milk and dried nonfat milk solids sold in the US are fortified with vitamin A to replace the vitamin A lost when the fat is removed (17). Fortified foods such as fortified breakfast cereals also provide vitamin A. Provitamin A carotenoids are abundant in darkly colored fruits and vegetables. Tables 4 and 5 at the end of this document list animal sources of vitamin A and a variety of plant sources of provitamin A carotenoids (18).

It is important for you to regularly eat foods that provide vitamin A or beta-carotene even though vitamin A is stored in the liver (2). Stored vitamin A will help meet needs when intake of provitamin A carotenoids or preformed vitamin A is low (19, 20).

What is the Recommended Dietary Allowance for vitamin A for children and adults?

The latest recommendations for vitamin A are given in the Dietary Reference Intakes developed by the Institute of Medicine. Dietary Reference Intakes (DRIs) is the umbrella term for a group of reference values used for planning and assessing diets for healthy people. One of those references values, the Recommended Dietary Allowance (RDA), is the average daily dietary intake level that is sufficient to meet the nutrient requirements of nearly all (97-98%) healthy individuals in each age and gender group (1). RDAs for vitamin A are listed as Retinol Activity Equivalents (RAE) to account for the different activities of retinol and provitamin A carotenoids. In the table below RDAs are also listed in International Units (IU) because food and some supplement labels list vitamin A content in International Units (1 RAE in micrograms (ug) = 3.3 IU). The RDAs for adults and children (21) in ug RAE and IUs are:

Table 1: Recommended Dietary Allowances for vitamin A in micrograms (ug) Retinol Activitiy Equivalents (RAE) and International Units (IUs) for children and adults

Age (years)	Children	Men	Women	Pregnancy	Lactation
1-3	300 ug or 1000 IU				
4-8	400 ug or 1333 IU				
9-13	600 ug or 2000 IU				
14-18		900 ug (3000 IU)	700 ug (2330 IU)	750 ug (2,500 IU)	1,200 ug (4,000 IU)
19+		900 ug (3000 IU)	700 ug or 2330 IU	770 ug (2565 IU)	1,300 ug (4335 IU)

Table 2: Adequate Intake for vitamin A in micrograms (ug) and **International Units (IU) for infants (21)**

There is insufficient information to establish a RDA for vitamin A for infants. An adequate intake (AI) has been established that is based on the amount of vitamin A consumed by healthy infants who are fed breast milk (21).

Age (months)	Males and Females
0 - 6	400 ug (1330 IU)
7 - 12	500 ug (1665 IU)

Results of two national surveys, the third National Health and Nutrition Examination Survey (NHANES III 1988-91) (1, 21) and the Continuing Survey of Food Intakes by Individuals (CSFII 1994) (1, 22) suggested that dietary intakes of some Americans do not meet recommended levels for vitamin A. These surveys highlight the importance of encouraging all Americans to include dietary sources of vitamin A in their daily diets.

There is no RDA for beta-carotene or other provitamin A carotenoids. The Institute of Medicine report suggests that consuming 3 to 6 mg of beta-carotene daily will maintain plasma beta-carotene blood levels in the range associated with a lower risk of chronic diseases (1). A diet that provides five or more servings of fruits and vegetables per day and includes some dark green and leafy vegetables and deep yellow or orange fruits should provide recommended amounts of beta-carotene.

When can vitamin A deficiency occur?

Vitamin A deficiency rarely occurs in the United States, but it is still a major public health problem in the developing world. At least 3 million children develop xeropthalmia, damage to the cornea of the eye, and 250,000 to 500,000 go blind each year from a deficiency of vitamin A (1). Most of these children live in developing countries. Night blindness is one of the first signs of vitamin A deficiency. In ancient Egypt it was known that night blindness could be cured by eating liver, which was later found to be a rich source of vitamin A (2). Vitamin A deficiency contributes to blindness by making the cornea very dry and promoting damage to the retina and cornea (23).

Vitamin A deficiency diminishes the ability to fight infections. In countries where immunization programs are not widespread and vitamin A deficiency is common, millions of children die each year from complications of infectious diseases such as measles. (9). When there is not enough vitamin A, cells lining the lung lose their ability to remove disease-causing microorganisms. This may contribute to the pneumonia associated with vitamin A deficiency (2.10.11).

There is increased interest in subclinical forms of vitamin A deficiency, described as low storage levels of vitamin A that do not cause overt deficiency symptoms. This mild degree of vitamin A deficiency may increase children's risk of developing respiratory and diarrheal infections, decrease growth rate, slow bone development, and decrease likelihood of survival from serious illness (8, 23, 24, 25). Children living in the United States who are considered to be at increased risk for subclinical vitamin A deficiency include:

- toddlers and preschool age children,
- children living at or below the poverty level,
- children with inadequate health care or immunizations,
- children living in areas with known nutritional deficiencies,
- recent immigrants or refugees from developing countries with high incidence of vitamin A deficiency or measles, and
- children with diseases of the pancreas, liver, intestines, or with inadequate fat digestion/absorption (9).

Vitamin A deficiency can occur when vitamin A is lost through chronic diarrhea and through an overall inadequate intake, as is often seen with protein-calorie malnutrition.

Low plasma retinol concentrations indicate depleted levels of vitamin A. This occurs with vitamin A deficiency but also can result from an inadequate intake of protein, calories and zinc. These nutrients are needed to make Retinol Binding Protein (RBP), which is essential for mobilizing vitamin A from your liver and transporting vitamin A to your general circulation (1).

Iron deficiency can also limit the metabolism of vitamin A, and iron supplements provided to iron deficient individuals may improve vitamin A nutriture as well as iron status (1).

Excess alcohol intake depletes vitamin A stores. Also, diets high in alcohol usually do not provide recommended amounts of vitamin A (1). It is very important for anyone who consumes excessive amounts of alcohol to include good sources of vitamin A in his or her diet. However, vitamin A supplementation may not be recommended for individuals who abuse alcohol because alcohol may increase liver toxicity associated with excess intakes of vitamin A (1,26). A medical doctor would need to evaluate this situation and determine the need for vitamin A supplementation.

Who may need extra vitamin A to prevent a deficiency?

Vitamin A deficiency rarely occurs in the United States, but the World Health Organization (WHO) and the United Nations International Children's Emergency Fund (UNICEF) issued joint statements about vitamin A and children's health. Both agencies recommend vitamin A administration for all children diagnosed with measles in communities where vitamin A deficiency is a serious problem and where death from measles is greater than 1%. In 1994, the American Academy of Pediatrics recommended vitamin A supplementation for two subgroups of children likely to be at high risk for subclinical vitamin A deficiency. These subgroups were children 6-24 months of age who had been hospitalized with measles and hospitalized children older than 6 months (27).

Fat malabsorption can promote diarrhea and prevent normal absorption of vitamin A. This is most often seen with cystic fibrosis, sprue, pancreatic disorders, and after stomach surgery. Healthy adults usually have a reserve of vitamin A stored in their livers and should not be at risk of deficiency during periods of temporary or short term fat malabsorption. Long-term problems absorbing fat, however, may result in deficiency, and in these instances physicians may advise vitamin A supplementation (9).

Vegetarians who do not consume eggs and dairy foods need greater amounts of provitamin A carotenoids to meet their need for vitamin A (1). It is important for vegetarians to include a minimum of five servings of fruits and vegetables daily and to regularly choose dark green leafy vegetables and orange and yellow fruits to consume recommended amounts of vitamin A.

What is the association between vitamin A, beta carotene and cancer?

Surveys suggest an association between diets rich in beta-carotene and vitamin A and a lower risk of some types of cancer (2, 28). There is evidence that a higher intake of green and yellow vegetables or other food sources of beta-carotene and/or vitamin A may decrease the risk of lung cancer (29). However, a number of studies that tested the role of beta-carotene supplements in cancer prevention did not find it to be protective (30). In a study of 29,000 men, incidence of lung cancer was greater in the group of smokers who took a daily supplement of betacarotene (31). The Carotene and Retinol Efficacy Trial, a lung cancer chemoprevention trial that provided randomized subjects with supplements of beta-carotene and vitamin A, was stopped after researchers discovered that subjects receiving beta-carotene had a 46% higher risk of dying from lung cancer than those who did not receive beta-carotene ((32). The Institute of Medicine (IOM) states that "beta-carotene supplements are not advisable for the general population," although they also state that this advice "does not pertain to the possible use of supplemental beta-carotene as a provitamin A source for the prevention of vitamin A deficiency in populations with inadequate vitamin A nutriture" (1).

Can an excess intake of vitamin A promote osteoporosis?

Osteoporosis, a disorder characterized by porous, weak bones, is a serious public health problem for more than 10 million Americans, 80% of whom are women. Another 18 million Americans have decreased bone density, which precedes the development of osteoporosis. Researchers have identified many factors that increase the risk for developing osteoporosis, including being female, thin, inactive, at advanced age, and having a family history of osteoporosis. An inadequate dietary intake of calcium, cigarette smoking and excessive intake of alcohol also increase the risk of developing osteoporosis.

Researchers are now examining a potential new risk factor for osteoporosis, an excess intake of vitamin A. Animal, human, and laboratory research suggest an association between greater vitamin A intake and weaker bones (33, 34). Researchers have also noticed that worldwide, the highest incidence of osteoporosis occurs in northern Europe, a population with a high intake of vitamin A (35). However, decreased biosynthesis of vitamin D associated with lower levels of sun exposure in this population may also contribute to this finding.

One small study of nine healthy individuals in Sweden found that the amount of vitamin A in one serving of liver may impair the ability of vitamin D to promote calcium absorption (36). To further test the association between excess dietary intake of vitamin A and increased risk for hip fracture, researchers in Sweden compared bone mineral density and retinol intake in approximately 250 women with a first hip fracture to 875 age-matched controls. They found that a dietary retinol intake greater than 1,500 mcg/day (more than twice the recommended daily intake for women) was associated with reduced bone mineral density and increased risk of hip fracture as compared to women who consumed less than 500 mcg per day (37).

This issue was also examined by researchers with the Nurses Health Study, who looked at the association between vitamin A intake and hip fractures in over 72,000 postmenopausal women. In this study, women who consumed the most vitamin A in foods and supplements (greater than or equal to 3000 mcg per day as retinol equivalents, which is over three times the recommended intake for adult men and women) had a significantly increased risk of experiencing a hip fracture as compared to those consuming the least amount. (less than 1250 mcg per day of retinol equivalents). The effect was lessened by use of estrogens but still raises questions about the effects of a high intake of vitamin A. In particular this raises questions about the effect of preformed vitamin A or retinol because retinol intake greater than 2000 mcg per day was associated with an increased risk of hip fracture as compared to a retinol intake less than 500 mcg (38).

A recent longitudinal study in more than 2,000 Swedish men was the first to measure blood levels of retinol to assess the risk of fractures in men. The investigators found that the risk of fractures was greatest in men with the highest serum retinol levels (greater than 75.62 mcg per d/l). The risk of fracture was further increased in men with the highest serum retinol levels. Men with retinol in the 99th percentile (greater than 103.12 mcg per d/l) had an overall risk of fracture that exceeded the risk among men with lower levels of serum retinol by a factor of seven. High vitamin A intake does not necessarily equate to high serum retinol; serum retinol is regulated by factors besides vitamin A intake, including age, gender, hormones and genetics. Serum beta carotene, however, was not associated with the risk of fracture. The researchers' findings, which are consistent with the results of studies in animals, as well as in vitro (laboratory studies) and epidemiologic dietary studies, suggest that intakes above the Upper Limit or approximately two times that of the RDA, may pose subtle risks to bone health that require further investigation. Vitamin D, which may contribute to osteoporosis, was not measured.

Additional clinical studies evaluating vitamin D and calcium as well as retinol for risk of fracture are warranted (39).

On the other hand, the Centers for Disease Control reviewed data from the Third National Health and Nutrition Examination survey (NHANES III), 1988-94, to determine whether there was any association between bone mineral density and fasting blood levels of retinyl esters, a form of vitamin A (40). Blood levels of retinyl esters in 5,800 participants were in the normal

range and researchers did not find any significant associations between bone mineral density and blood levels of retinyl esters. Additional research is needed to clarify the association between high levels of vitamin A intake and osteoporosis.

There is no evidence of an association between beta-carotene intake, especially from fruits and vegetables (many of which are naturally high in beta-carotene), and increased risk of osteoporosis. Current evidence points to a possible association with vitamin A as retinol only. If you have specific questions regarding your intake of vitamin A and risk of osteoporosis, it is recommended that you discuss this information with your physician or other trained health care practitioner to determine what's best for your personal health.

What is the health risk of too much vitamin A?

Hypervitaminosis A refers to high storage levels of vitamin A in the body that can lead to toxic symptoms. There are three major adverse effects of hypervitaminosis A:

- birth defects.
- liver abnormalities
- reduced bone mineral density that may result in osteoporosis (1)

Toxic symptoms can also arise after consuming very large amounts of preformed vitamin A over a short period of time. Signs of acute toxicity include nausea and vomiting, headache, dizziness, blurred vision, and muscular uncoordination (1, 7-9, 41, 42).

Although hypervitaminosis A can occur when very large amounts of liver are regularly consumed, most cases of vitamin A toxicity result from an excess intake of vitamin A in supplements. The Institute of Medicine has established Daily Tolerable Upper Levels (UL) of intake for vitamin A from supplements that apply to healthy populations (1). The UL was established to help prevent the risk of vitamin A toxicity. The risk of adverse health effects increases at intakes greater than the UL. The UL does not apply to malnourished individuals receiving vitamin A either periodically or through fortification programs as a means of preventing deficiency. It also does not apply to individuals being treated with vitamin A by medical doctors for diseases such as retinitis pigmentosa.

Table 3: Tolerable Upper Intake Levels (UL) for preformed vitamin A in micrograms (ug) and International Units (IU) for infants, children, and adults (1)

Age	Children	Men	Women	Pregnancy	Lactation
0-12 months	600 ug (2,000 IU)				
1-3 years	600 ug (2,000 IU)				
4-8 years	900 ug (3000 IU)				
9-13	1,700 ug (5665 IU)				
14-18 years		2,800 ug (9335 IU)	2,800 ug (9335 IU))	2,800 ug (9335 IU))	2,800 ug (9335 IU)
19+ years		3,000 ug (10,000 IU)	3,000 ug (10,000 IU)	3,000 ug (10,000 IU)	3,000 ug (10,000 IU)

Retinoids are compounds that are chemically similar to vitamin A. Over the past 15 years, synthetic retinoids have been prescribed for acne, psoriasis, and other skin disorders (43). Isotretinoin (Roaccutane[®] or Accutane[®]) is considered an effective anti-acne therapy. At very high doses, however, it can be toxic, which is why this medication is usually saved for the most severe forms of acne (44-46). The most serious consequence of this medication is birth defects.

It is extremely important for sexually active females who may become pregnant and who take these medications to use an effective method of birth control. Women of childbearing age who take these medications are advised to undergo monthly pregnancy tests to make sure they are not pregnant.

What is the health risk of too many carotenoids?

Nutrient toxicity traditionally refers to adverse health effects from a high intake of a particular vitamin or mineral. For example, large amounts of active, or preformed, vitamin A (naturally found in animal foods such as liver but also available in dietary supplements) can cause birth defects.

Provitamin A carotenoids such as beta-carotene are generally considered safe because they are not traditionally associated with specific adverse health effects. The conversion of provitamin A carotenoids to vitamin A decreases when body stores are full, which naturally limits further increases in storage levels. A high intake of provitamin A carotenoids can turn the skin yellow, but this is not considered dangerous to health.

Recent clinical trials that associated beta-carotene supplements with a greater incidence of lung cancer and death in current smokers raised concern about the effects of beta-carotene supplements on long-term health. However, conflicting studies make it difficult to interpret the health risk.

For example, the Physicians' Health Study compared the effects of taking 50 mg beta-carotene every other day to a placebo (sugar pill) in over 22,000 male physicians and found no adverse health effects (47). Also, a trial that tested the ability of four different nutrient combinations to inhibit the development of esophageal and gastric cancers in 30,000 men and women in China suggested that after 5 years those participants who took a combination of beta-carotene, selenium and vitamin E had a 13% reduction in cancer deaths (48).

One point to consider is that there may be a relationship between alcohol and beta-carotene because "only those men who consumed more than 11 g per day of alcohol (approximately one drink per day) showed an adverse response to B-carotene supplementation" in the lung cancer trial (1).

The Institute of Medicine did not set a Tolerable Upper Intake Level (UL) for carotene or carotenoids. Instead, they concluded that beta-carotene supplements are not advisable for the general population. As stated earlier, however, they may be appropriate as a provitamin A source or for the prevention of vitamin A deficiency in specific populations (1).

Selected Food Sources of vitamin A

As the 2000 Dietary Guidelines for Americans state, "Different foods contain different nutrients. No single food can supply all the nutrients in the amounts you need" (49). The following tables list a variety of dietary sources of vitamin A and provitamin A carotenoids. As the tables indicate, liver, eggs and whole milk are good animal sources of vitamin A. Many orange fruits and green vegetables are good sources of provitamin A carotenoids. Including these foods in your daily diet will help you meet your daily need for vitamin A. In addition, food manufacturers fortify a wide range of products with vitamin A. Breakfast cereals, pastries, breads, crackers, cereal grain bars and other foods may be fortified with 10% to 15% of the Daily Value (DV) for vitamin A. If you want more information about building a healthful diet, refer to the Dietary Guidelines for Americans http://www.ars.usda.gov/dgac (49) and the Food Guide Pyramid http://www.usda.gov/cnpp/pyramid2.htm (50).

Table 4: Selected Animal Sources of Vitamin A (18)

Animal sources of vitamin A provide the best absorbed form of this vitamin.

Food	IU/International Unit	% DV*
Liver, beef, cooked, 3 oz	30,325	610
Liver, chicken, cooked, 3 oz	13,920	280
Egg substitute, fortified, 1/4 cup	1,355	25
Fat free milk, fortified with vitamin A, 1 cup	500	10
Cheese pizza 1/8 of a 12-inch diameter pie	380	8
Milk, whole 1 cup	305	6
Cheddar cheese, 1 ounce	300	6
Whole egg, 1 medium	280	6

^{*} DV = Daily Value. DVs are reference numbers based on the Recommended Dietary Allowance (RDA). They were developed to help consumers determine if a food contains a lot or a little of a specific nutrient. The DV for vitamin A is 5,000 IU (1,500 micrograms retinol). Most food labels do not list a food's vitamin A content. The percent DV (%DV) listed on the table above indicates the percentage of the DV provided in one serving. Percent DVs are based on a 2,000 calorie diet. Your Daily Values may be higher or lower depending on your calorie needs. Foods that provide lower percentages of the DV also contribute to a healthful diet.

Table 5: Selected Plant Sources of Vitamin A (from beta-carotene) (18)

Plant sources such as beta carotene are not as well absorbed as animal sources of vitamin A especially when they are consumed whole and raw. However, they are still a valuable source of this vitamin.

Food	IU/International Units	% DV*
Carrot, 1 raw, 7 1/2 inches long	20,250	410
Carrots, boiled, 1/2-cup slices	19,150	380
Carrot juice, canned, 1/2 cup	12,915	260
Sweet potatoes, canned, drained solids, 1/2 cup	7,015	140
Spinach, frozen, boiled, 1/2 cup	7,395	150
Mango, raw, 1 cup sliced	6,425	130
Vegetable soup, canned, chunky, ready-to-serve	e, 1 cup 5,880	115
Cantaloupe, raw, 1 cup	5,160	105
Kale, frozen, boiled, 1/2 cup	4,130	80
Spinach, raw, 1 cup	2,015	40
Apricot nectar, canned, 1/2 cup	1,650	35

^{*} DV = Daily Value. DVs are reference numbers based on the Recommended Dietary Allowance (RDA). They were developed to help consumers determine if a food contains a lot or a little of a specific nutrient. The DV for vitamin A is 5,000 IU (1,500 micrograms retinol). The percent DV (%DV) listed on the nutrition facts panel of food labels tells adults what percentage of the DV is provided in one serving. Percent DVs are based on a 2,000 calorie diet. Your Daily Values may be higher or lower depending on your calorie needs. Foods that provide lower percentages of the DV also contribute to a healthful diet.

Table 5 (continued) Selected Plant Sources of Vitamin A (from beta-carotene) (18)

Food	IU/International Unit	% DV*
Oatmeal, instant, fortified, pl prepared with water, 1 packe		30
Tomato juice, canned, 6 ounc	ees 1,010	20
Apricots, with skin, juice pac 2 halves	k, 610	10
Pepper, sweet, red, raw, 1 ring 3 inches in diameter by 1/4-ir		10
Peas, frozen, boiled, 1/2 cup	535	10
Peach, raw, 1 medium	525	10
Peaches, canned, juice pack, 1/2 cup halves or slices	470	10
Papaya, raw, 1 cup cubes	400	8

^{*} DV = Daily Value. DVs are reference numbers based on the Recommended Dietary Allowance (RDA). They were developed to help consumers determine if a food contains a lot or a little of a specific nutrient. The DV for vitamin A is 5,000 IU (1,500 micrograms retinol). The percent DV (%DV) listed on the nutrition facts panel of food labels tells adults what percentage of the DV is provided in one serving. Percent DVs are based on a 2,000 calorie diet. Your Daily Values may be higher or lower depending on your calorie needs. Foods that provide lower percentages of the DV also contribute to a healthful diet.

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