

Periodontitis and Cavities

There are many good reasons to keep your teeth and gums healthy. Healthy teeth and gums not only look better, but they also promote better eating habits and nutrition. By contrast, unhealthy, inflamed gums are associated with various diseases, including coronary heart disease and an elevated risk for heart attack, while tooth loss is linked to malnutrition.

In a healthy mouth, the teeth are intact and anchored in pink, firm gums that do not bleed during brushing. A regular tooth care program should include flossing and brushing twice daily, as well as regular visits to the dentist for cleaning and examination.

Gum disease and tooth loss are especially common among the elderly. Some researchers believe that the malnutrition that afflicts older people may be in part due to poor dentition (the type, number, and arrangement of a set of teeth). In fact, some researchers believe that the short life span of early humans was related to tooth loss that caused starvation (Goodman AH 1989; Story R 1986).

The three most common problems in the oral cavity are dental caries (cavities) and the periodontal diseases gingivitis and periodontitis. These are caused by multiple factors, including plaque buildup, diet, oral hygiene, genetics, environment, and lifestyle factors. For more information on gingivitis, the most common dental disease, see the chapter titled *Gingivitis*. Dental caries and periodontitis are discussed in this chapter.

CAVITIES

Dental caries, or cavities, occur when microorganisms build up in deposits of dental plaque and ferment dietary sugars. The byproduct of this fermentation, lactic acid, lowers the pH at the junction of the plaque layer and tooth enamel, and eventually the enamel is eroded (Geddes DA 1991).

The layer of plaque in the mouth has recently been redefined as “biofilm” (Rudney JD 2000). Biofilm develops in a predictable pattern, whereby oral bacteria colonize areas of the gums and teeth, then spread and eventually link with other organisms in a cohesive film. This film can occur both above and below the gum line. If left intact, it may form a hard, mineralized mass called calculus (tartar) (Bernimoulin JP 2003). This is the hard, yellow substance that dentists scrape off with specialized equipment. Tartar contains masses of bacteria that produce lactic acid and promote tooth decay. Brushing and flossing alone cannot penetrate or remove the tartar.

One novel hypothesis for disrupting the creation of biofilm and preventing tartar involves oral vaccines that may protect the mouth against *Streptococcus mutans* (*S. mutans*), the bacteria most commonly responsible for dental cavities. Human studies have shown encouraging results with antibodies designed to suppress colonization of *S. mutans* in the biofilm (Michalek SM et al 2004).

The risk of developing cavities differs for each individual, based on factors such as oral hygiene, genetics, the size and shape of the teeth, resistance to infection, retention of dental plaque, and metabolism of sugar (Boraas J et al 1988; Conry J et al 1993). In addition, people with pre-existing conditions such as gum disease have a greater chance of developing cavities, and smoking can accelerate the transformation of plaque into tartar (Feldman R et al 1983). Other risk factors for dental cavities include exposure to lead (Watson G et al 1997), polychlorinated biphenyls (PCBs) (Rogan W et al 1988), and second-hand smoke (Aligne C et al 2003).

Clinically, cavities appear as blemishes on the tooth surface. If they are not clinically visible, they can still be detected using dental x-rays. Most dentists recommend one set of dental x-rays annually.

Waiting for tooth pain as a reason to visit the dentist is a not a good strategy for preventing cavities. In many cases, cavities are not painful because they affect only the surface layers of the tooth and do not extend into the dental pulp, which is the soft tissue inside the tooth. In more advanced cases, a cavity may extend into the pulp, causing intense pain and pulp disease known as pulpitis. Early pulpitis is generally treatable. If it is not treated, however, it can advance to pulp death. At this point, the tooth may stop hurting because the nerve has died. By the time a cavity has reached this stage, the tooth will most likely require extraction. Modern preventive dentistry is designed to prevent tooth decay from reaching such advanced stages.

Fluoride: Effective Against Cavities

Fluoride's role in preventing cavities has been extensively documented (Klein H 1972). Teeth with adequate fluoride are resistant to acid, and studies have shown a 30 percent to 50 percent reduction in decay following the fluoridation of drinking water (Neenan E et al 2004).

The use of fluoride, however, is not without its side effects. The most common side effect is known as fluorosis. This permanent alteration causes small, barely visible white flecks on adult teeth (Dean H 1934). It occurs early during tooth development, when adult teeth are just coming in (Den Besten P 1999). To help prevent it, experts recommend:

1. Use of low-fluoride water in infant formulas
2. Adult supervision of children during brushing
3. Rigid application standards when administering fluoride supplements to children (Fomon S et al 2000).

There is, however, little question that fluoride works to prevent cavities. When children between the ages of five and six were treated with a 1.2 percent fluoride gel versus a placebo gel twice daily, the fluoride group showed a 40 percent decrease in cavities compared to the placebo group after a two-year follow-up (Klein H 1972).

PERIODONTITIS

Periodontal diseases, including gingivitis and periodontitis, are inflammatory diseases that affect the supporting structures that anchor the teeth in place (periodontium). Gingivitis and periodontitis are related conditions: if left untreated, gingivitis, or inflammation of the gingival tissue (gums), can progress to periodontitis, a more serious condition. Gingivitis is a treatable and reversible condition, while periodontitis is an irreversible condition that can lead to tooth loss.

Risk factors for periodontitis include smoking, stress, depression (Grossi S 2000), and alcohol consumption (Tezal M et al 2004). Tobacco use is an important risk factor for periodontitis (Albandar JM et al 2000; Bergstrom J et al 2000a,b; Tomar S et al 2000). For more specific information on risk factors for gingivitis, the most common form of gum disease, see the chapter titled *Gingivitis*.

During periodontitis, the healthy gum tissue is transformed from pink and firm, with knife-edge margins between the soft tissue and the tooth, to inflamed and red. Eventually, the tissue pulls away from the tooth, allowing pockets to form. These pockets can be measured with a special probe during a standard dental check-up. Any pocket over 3 millimeters in depth signifies gingivitis; a pocket over 5 millimeters usually signifies periodontitis.

Periodontal infections frequently involve bacteria that discharge hydrogen sulfide, ammonia, amines, toxins, and inflammation-causing enzymes that can cause loss of tissue and teeth (Haffajee A et al 2000). Bleeding gums, bad breath, and pain also occur (Haffajee A et al 2000). Clinically, periodontitis is characterized by inflamed, red gums and deepening pockets between the tooth root and the gum tissue, as well as loss of bone in the jaw. Advanced periodontal disease can be diagnosed by changes in appearance of the teeth and gums, including:

1. noticeable loosening of the teeth
2. gum recession with the tooth root exposed
3. new spaces forming between the teeth
4. food being trapped between teeth and where gums have receded
5. constant bad taste in the mouth.

Periodontal disease is usually painless until late in the disease process, when the teeth are so loose that pain occurs while chewing. Retention of food in a pocket site may provoke a sudden burst of bacterial growth, resulting in a painful abscess (Loesche W et al 2001). At other times, the front teeth may become so loose that they separate.

Conventional therapy for periodontal disease consists of mechanical scaling and root planing, surgical treatment, and the use of various antimicrobial regimens (Loesche W et al 2001). The goal is to reduce the number of bacteria on the surface of the teeth by reducing the amount of plaque. If pocket depths in the gums are 5 millimeters or greater, large numbers of bacteria can accumulate that cannot be reached by normal oral hygiene. Periodontal surgery may then be recommended to reduce the pocket depths to 1 millimeter to 2 millimeters (Loesche W et al 2001).

Antibiotic therapy is sometimes needed when the bacterial count continues to climb. In open clinical trials, tetracycline has been used successfully to treat aggressive periodontitis, either as an oral tetracycline/surgery combination (Lindhe J et al 1984; Mandell R et al 1986, 1988) or alone for three to eight weeks (Christersson L et al 1993; Slots J et al 1983). Tetracycline can deplete calcium, magnesium, and iron, so people on tetracycline should also use a multivitamin (Pelton R et al 2001).

There are several ways to release medications directly into the periodontal pocket, including the use of long-lasting gels. These methods reduce the dose of medicine needed and deliver the antibiotic in a highly targeted fashion (Loesche W et al 2001). Devices that deliver localized antibiotics are about as effective as systemic agents in their ability to target harmful bacteria, and they are advantageous in that people do not have to remember to take the medicine, thus improving patient adherence (Loesche W 1993, 1999). These devices include Atridox®, PerioChip®, and Arestin® (Paper AP 2004).

Are Teeth Whiteners Safe?

Over the past decade, sales of at-home teeth-whitening products have exploded in the U.S. These products generally contain either hydrogen peroxide or carbamide peroxide, and are usually painted or brushed on, or applied in strips directly to the teeth. They are milder versions of whiteners that are used in the dentist's office, which may contain up to 35 percent active ingredients.

While studies have shown that these products do whiten teeth, there is some lingering concern about their safety. For example, studies have shown that peroxide from at-home whitening products penetrates the tooth enamel, into the pulpy interior of the teeth (Gokay O et al 2005). In studies of human molars, these products have also been shown to adversely affect the hardness of enamel (Leonard RH et al 2005; Basting RT et al 2005).

So far, however, no systemic adverse effects have been demonstrated with the use of teeth whiteners containing 10 percent carbamide peroxide (Li Y 2003). The most common side effects are moderate tooth sensitivity and mild gum irritation that usually discontinues when the product is no longer being used (Li Y 2003).

Because stronger at-home solutions containing up to 18 percent carbamide peroxide have not yet been extensively tested in humans, it may be advisable to use a milder at-home tooth-whitening product under a dentist's supervision.

TOOTH LOSS, NUTRITION, AND DIET

Approximately 60 percent of U.S. adults are missing at least one tooth, and 10 percent have no teeth at all (Marcus S et al 1996). Besides the aesthetic value of a nice smile, there are harmful health repercussions to lacking functional teeth, including a greater risk of malnutrition (ADA 2003). People who are missing their teeth have about 20 percent of the chewing capacity of people with teeth, and they tend to avoid eating fruits, vegetables, and whole grains (Moynihan P et al 2001). This can quickly lead to malnutrition and serious vitamin and mineral deficiencies.

GUM DISEASE, INFLAMMATION, AND CHRONIC DISEASE

Gum disease is clearly associated with heart disease and other health-related problems. This is not necessarily because of bacterial spread from the mouth into the bloodstream (as many people think). In fact, "bacteria showers" in the bloodstream are relatively common and occur in response to brushing teeth, bowel movements, and other normal activities. These are rarely dangerous for people with healthy immune systems. Rather, the link between gum disease and other systemic diseases appears to be due to an increased inflammatory response that occurs throughout the body and is triggered by inflammation in the gums. The following diseases have been associated with gum disease.

Infective Endocarditis. Infective endocarditis is a serious, potentially fatal bacterial infection of the heart or its valves or inner lining. It occurs when bacteria in the bloodstream are embedded on abnormal heart valves or damaged heart tissue. Dental procedures and diseases are associated with endocarditis in people with underlying congenital heart disease and in those who have prosthetic heart valves or have had other forms of heart surgery (Drangsholt M 1998; Lacassin F et al 1995; Van der Meer J et al 1992). About 8 percent of cases in the U.S. have been associated with periodontitis or other dental diseases without an associated dental procedure. Chances of infective endocarditis following dental procedures in people with pre-existing heart conditions ranged from 1 per 3000 procedures to 1 per 5000 procedures (Drangsholt M 1998). To prevent this condition, some heart patients are advised to take antibiotics during dental procedures.

Cardiovascular Disease. Studies have shown an association between periodontitis and cardiovascular disease (Beck J et al 1999; Loesche W et al 1988; Mattila K et al 1988), and suggest that periodontitis is a risk factor for cardiovascular disease (Loos BG et al 2000; Arbes S et al 1999; Beck J et al 1998). Periodontitis is linked to heart disease by inflammation. According to the latest research, large amounts of bacteria in the gums trigger a systemic inflammatory response, with elevated levels of pro-inflammatory chemicals such as COX (cyclooxygenase) products, arachidonic acid, and others. These pro-inflammatory chemicals may contribute to atherosclerosis, which is now understood to be an inflammatory disease that affects the inner linings of arterial walls (the endothelium). Numerous studies have thus linked inflammatory gum disease to cardiovascular events such as stroke, atherosclerosis, and thickening of calcifications in the carotid artery (Dorfer C et al 2004; Grau A et al 2004; Wu T et al 2000; Ravon N et al 2003; Beck J et al 2001).

Obesity. Obesity, a significant risk factor for numerous diseases, has been associated with periodontitis, gingivitis, and dental cavities (Wood N et al 2003). Other conditions associated with obesity such as metabolic syndrome or Syndrome X (a clustering of dyslipidemia, insulin resistance, hypertension, and type 2 diabetes) can worsen periodontitis (Grossi S et al 1998).

Diabetes. Periodontitis is twice as prevalent in diabetics as in non-diabetics (Loe H 1993). Experimentally produced periodontitis increased blood glucose levels in uncontrolled diabetic animals. Studies have linked the glycation and inflammation in diabetics to worsening periodontitis. Alternatively, studies have linked the inflammatory response triggered by worsening periodontitis to amplified glycation, a damaging process that links proteins to glucose molecules and has been implicated in hardening of the

arteries and other diseases (Grossi S et al 1998).

Osteoporosis. Significant relationships exist between periodontitis and osteoporosis (Jeffcoat M 1996, 1998; von Wowern N et al 1994; Streckfus C et al 1997; Ronderos M et al 2000; Tezal M et al 2000; Krook L 1972), and between tooth loss and osteoporosis (Krall E et al 1994, 1996; Tagushi A et al 1999; Grossi S et al 2000).

Pregnancy-Related Issues. Oral infections can increase the risk of low birth weight in newborns (March of Dimes 2000). Pregnant women with periodontitis were found to be 7.5 times more likely to have a pre-term, low-birth-weight infant than pregnant women without periodontitis (Offenbacher S et al 1996). Pregnancy can increase the frequency, severity, and degree of gingivitis (Hugoson A 1970; Loe H 1965).

Lung Disease. Poor oral hygiene provides an ideal growth environment for anaerobic bacteria, which can cause severe pneumonia, especially in people with impaired swallowing (Shreiner A 1979; Komiyama K et al 1985; Costerton J et al 1995; Mergran D et al 1986; Toews G 1986; Fiddian-Green R et al 1991; Levison M 1994; Moore W et al 2000; Appelbaum P et al 1978; Pratter M et al 1980; Scannapieco F 1999).

NUTRITION FOR A HEALTHY MOUTH

Good oral hygiene, regular tooth brushing and flossing, tongue cleaning, regular dental check-ups, and use of high-quality oral care products can prevent or reduce the risk of cavities. At the same time, because of the risk of a dangerous inflammatory response, it is important that people with gum disease protect themselves with powerful anti-inflammatories. The following nutrients protect the health of the gums and reduce inflammation.

Coenzyme Q10. In one study, topical application of CoQ10 to periodontal pockets significantly reduced gingivitis, bleeding of the gums, and pocket depths after five to seven days of treatment (Hanioka T et al 1994). In another study, symptoms of gingivitis and periodontitis improved three weeks after beginning CoQ10 treatment (Wilkinson E et al 1975). Topical application of CoQ10 improved adult periodontitis alone and in combination with non-surgical periodontal therapy (Hanioka T et al 1994).

Essential Oils. Mouth rinses containing essential oils such as eucalyptus oil and menthol significantly reduced both gingival inflammation and bleeding when used in conjunction with fluoride toothpaste (Beiswanger B et al 1997). Tea tree oil (*Melaleuca alternifolia*) is an antiseptic, fungicide, and bactericide that is effective against oral bacteria (Vasquez J et al 2002; Carson C et al 2001).

Folic Acid. Mouthwash containing folic acid is effective in treating gingivitis and its accompanying inflammation. Among pregnant women, who are prone to gingivitis, folate mouthwash has proven superior to oral folate supplementation in preventing gingivitis (Pack A 1980, 1984; Thompson M 1982).

Green Tea. Green tea extract is rich in a class of antioxidants called catechins. Two in particular, epigallocatechin gallate (EGCG) and epicatechin gallate (ECG), combat oral plaque and bacteria (Horiba N et al 1991; Otake S et al 1991; Rasheed A et al 1998). These green tea polyphenols work as anti-plaque agents by suppressing glucosyl transferase, which oral bacteria use to feed on sugar. Other research has demonstrated that green tea extract can kill oral bacteria and inhibit collagenase activity. Collagenase, a natural enzyme that becomes overactive in the presence of bacterial overgrowth, can destroy healthy collagen in gum tissue.

Green tea extract applied topically inhibits *S. mutans* bacteria in the laboratory. These bacteria have been implicated in the development of dental cavities. The scientists suggested that certain extracts from green tea might be especially helpful in preventing tooth decay by inhibiting the development of bacterial plaque (Hattori M et al 1990). In a Chinese study, green tea extract was used to rinse and brush the teeth. The study demonstrated that *S. mutans* could be inhibited completely after contact with green tea extract for five minutes. There was no drug resistance after repeat cultures, and the researchers concluded that green tea extract is effective in reducing the risk of developing cavities (You SQ 1993). Other studies have found that the catechins in green tea remain at active levels in saliva for up to one hour following application (Tsuchiya H et al 1997).

More recent studies confirm the benefits of green tea in fighting gum disease, especially when combined with conventional treatments. In a pilot study, hydroxypropylcellulose strips containing green tea catechins as a slow-release local delivery system were applied to the pockets in periodontal patients once a week for eight weeks. The green tea catechins inhibited the bacteria *P. gingivalis* and *Prevotella spp* ., and a reduction in pocket depth was observed (Hirasawa et al 2002).

Aloe Vera. Aloe vera gel packings are sometimes used by dentists after tooth extraction to reduce the incidence of infection and dry socket (Poor M et al 2002). They have also been shown to reduce the risk of developing ulcers in the mouth (Garnick J et al 1998).

Propolis. A 20 percent ethanol propolis extract was compared to antifungal agents such as nystatin, clotrimazole, econazole, and fluconazole in a study designed to assess the susceptibility of *Candida albicans* , an oral bacteria. The researchers concluded that the propolis extract could be an alternative medicine in treating candidiasis, but further studies were needed (Martins RS et al 2002)

For More Information...

Additional chapters that may be of interest include:

- Atherosclerosis
- High Homocysteine
- Type 2 Diabetes

Vitamin C has long been known for its ability to prevent gum disease and tooth loss. In fact, the use of vitamin C in dental disease is one of the earliest recorded uses of nutrient therapy in Western medicine. In 1747, a British Naval physician named James Lind noticed that lime juice, which is rich in vitamin C, helped prevent scurvy, which causes tooth loss. As a result, British sailors bottled lime juice for gum disease prevention. Incidentally, this practice later gave rise to the term “Limey.”

Modern studies have confirmed the value of vitamin C, in conjunction with other antioxidants, in promoting good oral health. In one controlled, double-blind study of patients with periodontitis, a multivitamin combined with regular brushing resulted in significant improvements in gum health and a reduction in pockets after 60 days (Munoz C et al 2001). Clinical studies of people with vitamin C deficiencies show that gingival inflammation is directly related to ascorbic acid status, suggesting that ascorbic acid may influence the early stages of gingivitis, particularly bleeding (Leggott P et al 1986).

Researchers have also examined the value of vitamin D and calcium, which are typically used to reduce the risk of osteoporosis. Supplementation with these two nutrients reduces the rate of bone and tooth loss in postmenopausal women and men. Calcium intake of 800 mg or more per day reduced the risk of periodontitis in females (Nishida M et al 2000).

REDUCING GUM-RELATED INFLAMMATION

Because of the association between gum disease and systemic inflammation, researchers have begun looking at anti-inflammatory nutrients in the context of gum disease. In one study, 30 adults with gum disease were given a variety of polyunsaturated fatty acids, including omega-3 fatty acids from fish oil (up to 3000 mg daily) and omega-6 fatty acids from borage oil (up to 3000 mg daily). At the end of the study, clinically significant improvements were measured in both gingival inflammation and the depth of gum pockets (Rosenstein ED et al 2003). Another preliminary human study found that omega-3 fatty acids tended to reduce inflammation, but called for more thorough research (Campan P et al 1997). However, in light of the established connection between omega-3 and omega-6 fatty acids and inflammation, and the fatty acids' lack of side effects, it is reasonable for people with gum disease to consider using these supplements. Other anti-inflammatory supplements include ginger and curcumin, though neither of these has been studied in the context of inflammatory gum disease.

LIFE EXTENSION FOUNDATION RECOMMENDATIONS

Good oral health begins with a disciplined program of flossing, twice-daily brushing, and tongue cleaning with a tongue scraper to remove plaque and bacteria colonies on the tongue before they become incorporated in the biofilm. It is also important to visit a dentist for professional cleanings at least twice a year, and perhaps even more often. Because of the radiation associated with x-rays, Life Extension does not recommend annual dental x-rays, although occasional dental x-rays are necessary.

Avoid behaviors that contribute to gum disease and tooth decay, especially tobacco use and consumption of refined sugar. Instead, focus on consuming a diet rich in fruits and vegetables that provide important phytochemicals and nutrients. In addition, patients with gum disease and existing heart disease should monitor their levels of inflammation. C-reactive protein and homocysteine are both indicators of inflammation, which can be determined by blood tests. For more information on comprehensive blood testing, call 1-800-544-4440.

Your choice of toothpaste is also important. Today, the market is flooded with very strong toothpastes that contain high levels of hydrogen peroxide. A toothpaste is now available that has been fortified with coenzyme Q10, folic acid, tea tree oil, and other nutrients that are directly delivered to the gums each time one brushes. This novel toothpaste also contains a mild solution of 0.2 percent hydrogen peroxide.

A mouthwash containing tea tree oil, peppermint, eucalyptus, and other soothing nutrients may also be helpful. A mouth spray called MistOral III™ contains CoQ10, vitamin E, camu camu, peelu, vitamin K1, gotu kola extract, propolis extract, and many other herbal ingredients. The recommended daily usage is to spray this along the gum lines and swish it through the mouth and teeth several times.

In addition, a number of nutrients have been shown to improve oral health, including:

- **Coenzyme Q10**—100 milligrams (mg) daily
- **Folic acid**—400 micrograms (mcg) to 800 mcg daily
- **Green tea extract**—725 mg daily (93 percent polyphenols)
- **Vitamin C**—2 to 4 grams (g) a day (taken as 500 mg every few hours)
- **Calcium**—1200 mg to 1500 mg daily
- **Vitamin D**—800 IU to 1000 IU daily
- **Omega-3 fatty acids**—Up to 3000 mg daily of EPA/DHA
- **Omega-6 fatty acids**—Up to 3000 mg daily of GLA

Patients with mouth sores (ulcers) should consider using **aloe vera** gel packs.

PERIODONTITIS AND CAVITIES SAFETY CAVEATS

An aggressive program of dietary supplementation should not be launched without the supervision of a qualified physician. Several of the nutrients suggested in this protocol may have adverse effects. These include:

Calcium

- Do not take calcium if you have hypercalcemia.
- Do not take calcium if you form calcium-containing kidney stones.
- Ingesting calcium without food can increase the risk of kidney stones in women and possibly men.
- Calcium can cause gastrointestinal symptoms such as constipation, bloating, gas, and flatulence.
- Large doses of calcium carbonate (12 grams or more daily or 5 grams or more of elemental calcium daily) can cause milk-alkali syndrome, nephrocalcinosis, or renal insufficiency.

Coenzyme Q10

- See your doctor and monitor your blood glucose level frequently if you take CoQ10 and have diabetes. Several clinical reports suggest that taking CoQ10 may improve glycemic control and the function of beta cells in people who have type 2 diabetes.
- Statin drugs (such as lovastatin, simvastatin, and pravastatin) are known to decrease CoQ10 levels.

EPA/DHA

- Consult your doctor before taking EPA/DHA if you take warfarin (Coumadin). Taking EPA/DHA with warfarin may increase the risk of bleeding.
- Discontinue using EPA/DHA 2 weeks before any surgical procedure.

Folic acid

- Consult your doctor before taking folic acid if you have a vitamin B12 deficiency.
- Daily doses of more than 1 milligram of folic acid can precipitate or exacerbate the neurological damage caused by a vitamin B12 deficiency.

Green Tea

- Consult your doctor before taking green tea extract if you take aspirin or warfarin (Coumadin). Taking green tea extract and aspirin or warfarin can increase the risk of bleeding.
- Discontinue using green tea extract 2 weeks before any surgical procedure. Green tea extract may decrease platelet aggregation.
- Green tea extract contains caffeine, which may produce a variety of symptoms including restlessness, nausea, headache, muscle tension, sleep disturbances, and rapid heartbeat.

Vitamin C

- Do not take vitamin C if you have a history of kidney stones or of kidney insufficiency (defined as having a serum creatine level greater than 2 milligrams per deciliter and/or a creatinine clearance less than 30 milliliters per minute).
- Consult your doctor before taking large amounts of vitamin C if you have hemochromatosis, thalassemia, sideroblastic anemia, sickle cell anemia, or erythrocyte glucose-6-phosphate dehydrogenase (G6PD) deficiency. You can experience iron overload if you have one of these conditions and use large amounts of vitamin C.

Vitamin D

- Do not take vitamin D if you have hypercalcemia.
- Consult your doctor before taking vitamin D if you are taking digoxin or any cardiac glycoside.
- Only take large doses of vitamin D (2000 international units or 50 micrograms or more daily) if prescribed by your doctor.
- See your doctor frequently if you take vitamin D and thiazides or if you take large doses of vitamin D. You may develop hypercalcemia.

- Chronic large doses (95 micrograms or 3800 international units or more daily) of vitamin D can cause hypercalcemia.

For more information see the Safety Appendix

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