

Chapter 1

The Essentials of Vitamin D

In This Chapter

- ▶ Getting the lowdown on vitamin D
 - ▶ Making the connection between vitamin D and your health
 - ▶ Exploring the origins of vitamin D
 - ▶ Reaping the medical benefits of vitamin D
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You think you have enough vitamin D in your body? You're in for a surprise. You think you know what vitamin D does for you? You're in for a shock. Many people don't have enough vitamin D, and almost nobody knows all that it might do for you. In fact, even I don't know everything it does for you because scientists are discovering new possible roles for it almost daily.

If vitamin D were a house, it might be the most desirable house on the block. It's turning out to provide possible benefits for your body that you could never have imagined. In this chapter, you discover what vitamin D is and what it does for you.

Understanding What Vitamin D Is and How It Works

When is a vitamin not a vitamin? When it's vitamin D.

A *vitamin* is defined as an essential nutrient that a living being must acquire in tiny amounts from the diet. A vitamin is a chemical that's essential for your body but that your body can't make; it must be ingested. By this definition, vitamin D isn't a vitamin at all. Consider this — your skin can make vitamin D when it's exposed to sunlight, so your body doesn't have to acquire it from food.

If vitamin D isn't really a vitamin, what is it? It becomes a hormone called *calcitriol* (active vitamin D) after your body metabolizes it. A *hormone* is a chemical in your body that regulates your physiology.

But old names are hard to change, so even though the substance I talk about throughout this book can be made in your skin and becomes a hormone, I (and other experts around the world) still call it vitamin D.

In the following sections, I explain how vitamin D is formed in the skin, how the body turns it into a hormone, and how the vitamin D hormone (calcitriol) affects your body.

Forming vitamin D in the body

Vitamin D comes in two forms:

- ✓ **Vitamin D₂**: The form found in plants
- ✓ **Vitamin D₃**: The form found in animals

Both forms of vitamin D are created when the ultraviolet rays of the sun act upon a form of cholesterol. In certain plants, the ultraviolet rays convert a molecule called ergosterol into vitamin D₂, which is also called ergocalciferol. In humans, vitamin D starts as a substance in the skin called *7-dehydrocholesterol*. The ultraviolet B rays from the sun convert 7-dehydrocholesterol into vitamin D₃, or *cholecalciferol*.

However, neither vitamin D nor vitamin D₃ are active yet. In fact, vitamin D does nothing by itself; it's completely inactive, and that may make you wonder what all the fuss is about. But it's what vitamin D turns into that becomes important. Vitamin D travels through the bloodstream to the liver, where it's turned into 25-hydroxycholecalciferol (25(OH)D or *calcidiol*). This is a prohormone or precursor for the vitamin D hormone. The vitamin D prohormone travels through the bloodstream to the kidneys, where it's turned into the active form, 1,25-dihydroxycholecalciferol (1,25(OH)₂D₃ or *calcitriol*). 1,25(OH)₂D₃ is the active vitamin D hormone. It is released back into the bloodstream where it then regulates how your body uses calcium and phosphorus. Figure 1-1 shows the conversion process in the body. Figure 1-2 shows the chemical reaction.

Some controversy has arisen over whether vitamin D₂ is as active as vitamin D₃ when it's ingested, but the consensus is that D₃ is two or three times as potent in raising the level of 25-hydroxycholecalciferol.

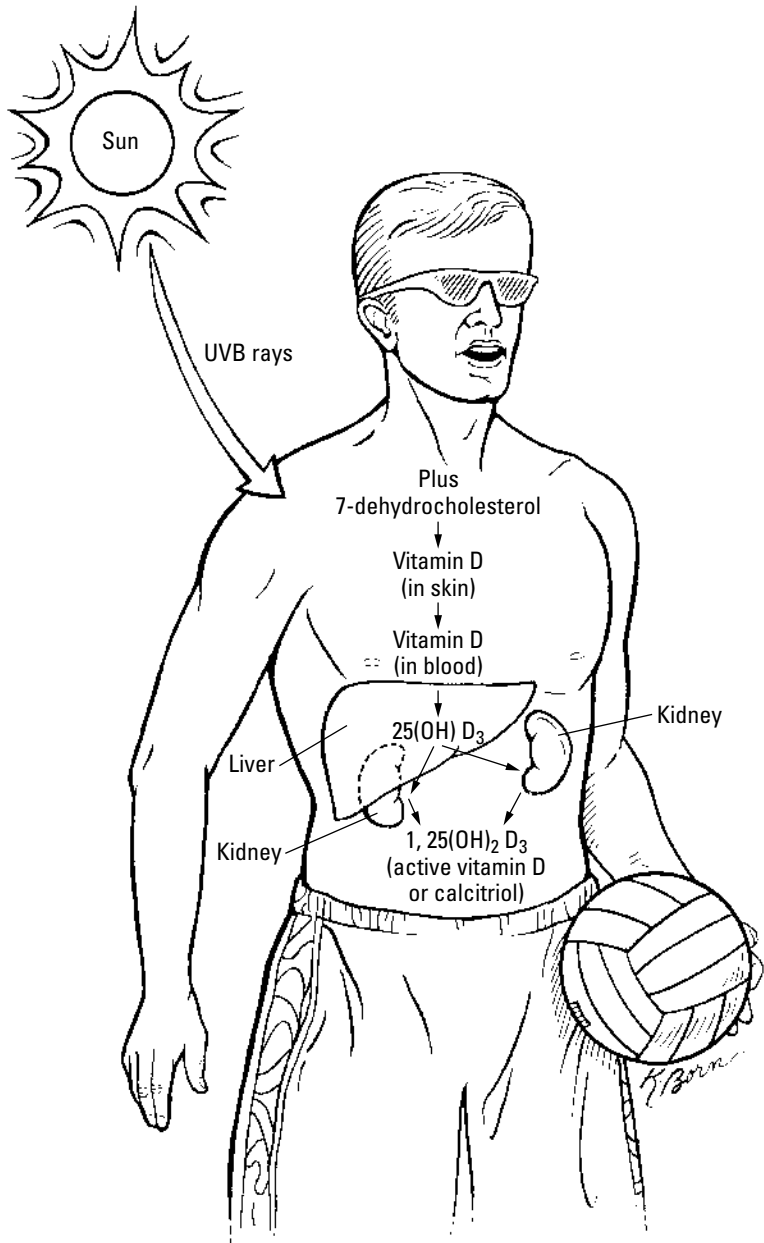


Figure 1-1: How the body creates vitamin D.

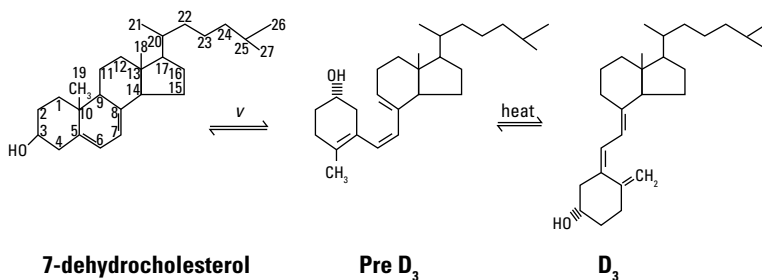


Figure 1-2: Conversion of 7-dehydrocholesterol to vitamin D₃ in the skin.



Because the liver and the kidneys are involved in the production of calcitriol, diseases of these organs may affect your ability to make this hormone.

Although the kidneys produce most of the calcitriol that ends up in the blood, there is some evidence that the conversion of 25(OH)D₃ into 1,25(OH)₂D₃ may occur in other tissues in the human body. The production of calcitriol in these tissues is low in comparison to the kidney, and calcitriol made in these tissues is probably not released back into the serum. This calcitriol acts within the tissue where it's made:

- ✓ Cells of the immune system (macrophages, dendritic cells)
- ✓ Brain
- ✓ Breast
- ✓ Colon (large intestine)
- ✓ Endothelial cells (inner lining of blood vessels)
- ✓ Pancreas
- ✓ Parathyroid glands
- ✓ Placenta
- ✓ Prostate
- ✓ Skin



Throughout this book, when I say “active vitamin D” or calcitriol, I’m referring to 1,25(OH)₂D₃. It’s easier for your brain to digest “active vitamin D” instead of the string of scientific notation.

Regulating the production of vitamin D

Several factors strictly control the amount of active vitamin D produced in the kidneys and in other tissues. The biggest factor is the result of self-regulation. As the amount of calcitriol increases, it blocks the production of more calcitriol.

Another important substance that stimulates the production of calcitriol is the circulating amount of another hormone called parathyroid hormone. When blood calcium levels fall, parathyroid hormone levels increase and this promotes the conversion of $25(\text{OH})\text{D}_3$ into calcitriol within the kidneys. Concentrations of calcium and phosphate in the blood also control the production of calcitriol by the kidneys even without parathyroid hormone. As the calcium and phosphate levels fall, they stimulate the production of calcitriol in the kidneys.

The production of active vitamin D in organs and tissues other than the kidneys normally doesn't spill over into the bloodstream to raise the active vitamin D in the blood. For example, during pregnancy the placenta makes calcitriol but at best a negligible amount enters the maternal circulation (pregnant women without kidneys have very low calcitriol levels despite the placenta making calcitriol). However, in certain diseases, such as sarcoidosis (a disease where swelling occurs in the lymph nodes, lungs, liver, skin, and other tissues), immune cells called macrophages produce so much calcitriol that it spills over into the bloodstream and causes increased calcium in the blood.

Moving vitamin D around the body

Vitamin D, $25(\text{OH})\text{D}_3$, and calcitriol are carried in the blood by a vitamin D-binding protein. This protein is necessary because these substances aren't water soluble and can't dissolve in blood. (Vitamin D dissolves in fat.) Ninety-nine percent of all the different forms of vitamin D are bound to the vitamin D binding protein, and only 1 percent is free to enter cells.

The different forms of vitamin D that are bound to the vitamin D binding protein are protected from destruction by cells and excretion by the kidneys. Only the 1 percent that's free is available to carry out the functions of active vitamin D.

Pregnancy and estrogen use are a few conditions that can result in increased production of vitamin D-binding protein. These conditions cause the body to make more active vitamin D to take up all the extra binding sites, but the amount that's free and able to enter cells usually remains normal. Calcitriol levels more than double during pregnancy but it's only in the third trimester that free levels of calcitriol increase above normal.

Putting vitamin D to work

The best-understood role for the calcitriol is in the control of how your body uses calcium and phosphorus to make strong bones. However, research is showing that many organs and systems in your body may also need active vitamin D. The intestine and bones rely on the kidneys to make and ship calcitriol to them. However, the other organs that need calcitriol may be able to make small amounts on their own.

Vitamin D's effects on your cells

Calcitriol has two different ways to influence cells: a genomic action, which may take hours to days to occur, and a rapid response, which can occur in minutes.

In genomic action, calcitriol binds to the vitamin D receptor and together the active vitamin D and its receptor attach to the DNA. This interaction affects the activity of more than 500 genes. (Part II discusses some of the consequences.) Each of these genes produces a protein; some of these proteins regulate calcium and bone metabolism whereas others may help protect cells from cancer, influence insulin secretion, and affect the immune response.

The rapid responses don't result from attachment of the vitamin D receptor to the genes in the nucleus. Here are three examples of rapid responses:

- ✔ White blood cells take up calcium rapidly when calcitriol is added. This action takes place when calcitriol and its receptor attach to the membrane that surrounds the cell.
- ✔ Calcitriol also protects skin cells from the damaging effects of ultraviolet irradiation. This effect may be the function of other substances produced when vitamin D forms in the skin.
- ✔ The rapid uptake of calcium from the intestine is considered to be another example of a rapid response, as is the rapid secretion of insulin in response to glucose.

These rapid responses have only been studied in cultured cells, not in the body.

Active vitamin D works by entering cells and attaching to a protein called the *vitamin D receptor*, located in the nucleus of cells, where the genetic material is located. This combination of calcitriol and its receptor stimulates the cell to make proteins that regulate the way the body works. For example, some of the proteins produced in response to calcitriol in the intestine help transport calcium across the intestine and into the bloodstream, greatly increasing the absorption of calcium from the diet. The vitamin D receptor is found in several cells that are critical for controlling the metabolism of calcium, phosphorus, and bone: intestinal cells, bone cells, kidney cells, and parathyroid gland cells.

Vitamin D receptors also are present in most other tissues, including the brain, heart, skin, ovary and testicle, prostate gland, and breast, as well as the cells of the immune system, including white blood cells and other key immune cells (see Chapter 5). In fact, at least 33 different tissues contain the vitamin D receptor:

- | | |
|---------------------------|----------------------------------|
| ✓ Adipose (fat) | ✓ Muscle, smooth |
| ✓ Adrenal | ✓ Osteoblast (bone-forming cell) |
| ✓ Bone | ✓ Ovary |
| ✓ Bone marrow | ✓ Pancreas |
| ✓ Brain | ✓ Parathyroid |
| ✓ Breast | ✓ Parotid |
| ✓ Cartilage | ✓ Pituitary |
| ✓ Colon (large intestine) | ✓ Placenta |
| ✓ Epididymis | ✓ Prostate |
| ✓ Hair follicle | ✓ Retina |
| ✓ Kidney | ✓ Skin |
| ✓ Liver | ✓ Small intestine |
| ✓ Lung | ✓ Stomach |
| ✓ Lymphocytes | ✓ Testis |
| ✓ Muscle, embryonic | ✓ Thymus |
| ✓ Muscle, heart | ✓ Thyroid |
| | ✓ Uterus |

Seeing How Vitamin D Affects Your Health

The medical community has known of the benefits of vitamin D on bone health for decades. In more recent years, scientists have discovered that vitamin D may play a role in many other aspects of our health. In the following sections, I give you an overview of some of the most promising areas in which vitamin D may improve health and prevent diseases.

Building bone

The work of calcitriol is intimately linked to the way your body uses calcium. Active vitamin D levels increase when you regularly eat a diet low in calcium. When elevated, the role of calcitriol begins in the intestine, where it promotes increased absorption of calcium in an effort to overcome your low dietary calcium intake. Calcitriol also influences the kidneys, where it keeps calcium from leaving in the urine. Finally in the skeleton, calcitriol causes both the production of the framework of the bone and the mineralization of that framework with calcium and phosphate. On the other hand, abnormally high levels of calcitriol cause bone to break down and too much calcium to be absorbed by the intestines; this can cause toxic levels of blood calcium.

Normal levels of calcitriol promote the breakdown of old bone and the creation of new bone. Another way that calcitriol protects bone is by influencing the production of the parathyroid hormone. If you have a deficiency of vitamin D, you can't make enough calcitriol. As a result the parathyroid gland makes more parathyroid hormone which goes to bone and breaks it down to release calcium into the bloodstream. If this goes on too long, the increase in parathyroid hormone is detrimental, leading to weakened bones. Restoring vitamin D and calcitriol levels to normal allows the skeleton to regain lost calcium and strength. Maintaining the calcium level in the blood is important for the body's muscle function: heart muscles, skeletal muscles, and all other muscles. (Check out Chapter 4 for more on bones, teeth, and vitamin D.)



As they grow, children add more bone than they break down, so bone mass increases. When you're a kid, calcium absorption from the diet has to be very efficient to meet the needs of growing bone, so active vitamin D is very important at this stage of life. When you stop growing, there is still a lot of activity going on in the bone. About 10 to 30 percent of the bone in your body is renewed each year. After you reach your 30s, you begin to lose slightly more

bone than the amount you make, so you have a net loss of bone. At menopause women lose bone mass even more rapidly. Because of all this bone loss during adulthood you need to build up plenty of bone at a younger age so that by the time you start to lose more bone mass than you gain, you can avoid *osteoporosis*, a condition in which the bones are fragile and can fracture.

Reducing your risk of cancer

One of the most promising new roles for vitamin D is in the prevention of cancer. In some studies, the rates of certain but not all cancers appear to be lower the closer you live to the equator. Some scientists think that this is because you make more vitamin D in your skin the closer you live to the equator. Other studies even show that high blood levels of vitamin D are associated with lower rates of a number of cancers. Based on this they estimate that higher blood vitamin D levels could cause:

- ✔ A 50 percent reduction in the risk of colon cancer
- ✔ A 30 percent reduction in the risk of breast cancer
- ✔ A 30 percent reduction in the risk of ovarian cancer
- ✔ A 43 percent reduction in the risk of pancreatic cancer

There are some other bits of evidence that suggest this is true. For example, calcitriol has been shown to slow the growth of cancer cells isolated from the breast, the prostate, and the colon, and it can kill cancer cells in culture. (See Chapter 6 for more specifics.) Unfortunately we don't know if this ability to slow or even kill cancer cells occurs in humans. Also, the high doses of calcitriol needed in cell culture studies would cause toxic, high levels of blood calcium if they were used in humans. Because of this scientists are currently making calcitriol-like drugs that have similar anti-cancer properties in cell cultures as active vitamin D but that avoid the effects of calcitriol on bone and calcium metabolism. That way, doctors could give very high doses of such a compound without risking the toxic side effect of high calcium.

Preventing heart disease and diabetes

Still other studies are pointing to a possible role for high blood vitamin D levels in the prevention of other chronic diseases like diabetes and heart disease. If you looked at a graph comparing the average blood pressure of the population with the distance from

the equator, you'd see that blood pressure rises the farther you get from the equator and its strong sun rays (and, therefore, greater skin production of vitamin D). Of course, the change in blood pressure might have nothing to do with vitamin D, but it seems reasonable to assume that it does.

Studies in animals show that calcitriol can lower blood pressure and decrease the risk of an enlarged heart. Calcitriol also relaxes blood vessels, which further lowers blood pressure. (Flip to Chapter 7 for more on how vitamin D helps maintain your cardiovascular system.)

There is also evidence that higher blood vitamin D levels might also protect against the development of diabetes. This might be related to observations that calcitriol can alter the cells of the immune system to suppress autoimmunity, the reaction of the body against itself (see Chapter 5). Type 1 diabetes mellitus is an autoimmune disease, so active vitamin D might help limit the development of this disease. At the same time, studies in animals and cell cultures suggest that calcitriol active vitamin D improves insulin secretion from the pancreas and increases the sensitivity of cells to the action of insulin. These actions might help prevent and treat type 2 diabetes. (Chapter 8 explains the connection between vitamin D and diabetes.)

Checking Out Where Vitamin D Comes From

Outside the body, vitamin D comes from three major sources:

- ✓ The sun
- ✓ Food
- ✓ Supplements

Part III delves into these sources in detail, but I make a few general remarks here.

Sun

The sun has provided vitamin D for thousands of years. However, the sun is also known to cause skin cancer, photo-damage, wrinkles, and other problems. The challenge is striking the right balance

between getting enough sun for your vitamin D needs and avoiding sun damage (see Chapter 11 for details). Even still, most dermatologists believe that there is no “safe” level of sunlight exposure and that the sun should not be relied upon as a source of vitamin D.

Four major factors determine the effect of sunlight on your vitamin D level:

- ✔ **Time of year:** In the summer, the sun’s rays are more direct. Direct rays much more effectively raise your skin production of vitamin D.
- ✔ **Your latitude on the Earth:** Latitudes closer to the equator get direct sunlight for a longer time each day and for more months out of the year.
- ✔ **Obstacles to sun exposure of your skin:** Whether it be clouds, dark skin color, smog, a hat, an umbrella, or suntan lotion, anything that limits the exposure of your skin to ultraviolet light significantly reduces your production of vitamin D in the skin.
- ✔ **Altitude:** The higher you are, the less atmosphere there is to block the sun’s rays.



Any factor that reduces the amount of ultraviolet light that reaches your skin will reduce the amount of vitamin D produced there.

Food

Only a few foods contain enough vitamin D to make eating them solely for this reason worthwhile. Food manufacturers are fortifying many foods with extra vitamin D. At the present time, vitamin D-fortified foods can provide enough vitamin D only for babies and toddlers, whose requirements are relatively small. In Chapter 12, I tell you what you need to know about foods and vitamin D.

Supplements

With the tremendous growth of knowledge about vitamin D and its effects, there has come an abundance of supplements in every size, shape, and form. If you can’t get enough vitamin D from your diet, you can get all the vitamin D you need from supplements. Chapter 13 tells you how to use pills to meet your vitamin D needs.

Appreciating the Long-Term Medical Benefits

Vitamin D plays a huge role in your health. The most important area in the past has been bone health in children and adults, but many researchers think that vitamin D's other functions may be equally important.

Prevention of deformity

The major and most well-known role of vitamin D over the years has been preventing rickets in children. When vitamin D isn't present in sufficient amounts during growth, the bones don't lengthen properly or become properly mineralized. As a result, the weight of the body makes the bones become curved, deformed, painful, and tender, and they fracture easily — a condition known as *rickets*. Rickets affects all bones, including the teeth and the spine. Vitamin D is also essential for normal development and maintenance of muscles, and in rickets the muscles are greatly weakened, tender, and sore. (Chapter 4 provides the information you need to avoid rickets.)

When rickets occurs in adults it's called osteomalacia, and it doesn't lead to deformity because the bone structure has already formed. It does, however, lead to weak bones and muscles, and pain in muscles and bones that responds to vitamin D.

Rickets was a rare disease until many people began to leave farms and migrate to cities during the Industrial Revolution. The sun didn't penetrate the pollution as easily, and people stayed indoors most of the day. Nowadays, rickets is still rare in many places; however, it's making a comeback in racial groups with dark skin and in places where people cover up their skin for religious or social reasons. In fact, some of the lowest vitamin D levels are seen in countries close to the equator where typical outdoor clothing has the head and entire body covered.



Unless the mother takes a very high dose (4,000 to 6,400 IU per day) supplement of vitamin D, human breast milk contains little or no vitamin D. As a result babies who are exclusively breastfed are more likely to become deficient than babies who receive vitamin D-fortified baby formulas. Also, babies born of mothers who were low in vitamin D during pregnancy are even more likely to develop rickets in the weeks to months after birth.

Lives saved?

Some scientists feel that the value of vitamin D in health has been underestimated. However, it's hard to estimate the effects of vitamin D, for several reasons:

- ✔ The experts don't agree on what constitutes "sufficient levels" of vitamin D in your blood.
- ✔ All of vitamin D's various contributions to health aren't fully known.
- ✔ Controversy exists over whether some of the proposed non-bone effects of vitamin D are real, particularly those effects on chronic diseases that take years to develop, like cancer, heart disease, and diabetes. For example, some studies have shown that a lower intake of vitamin D is associated with a higher risk of heart disease. This could be because the people that took less vitamin D may also have exercised less, smoked more, and had other poor lifestyle habits. A definitive answer requires conducting a study that randomly compares two similar groups — one that gets the vitamin and the other that doesn't.

Although these randomized studies are very expensive and hard to do, fortunately a large randomized study called VITAL is under way in the USA which is testing the effects of vitamin D on cancer and heart disease outcomes. So we may have a definitive answer to these questions as to whether vitamin D prevents heart disease and cancer in the next five years or so.

In the meantime, by using studies that associate serum vitamin D levels to the risk that a person may develop a disease, and assuming that the low vitamin D is causing the disease of interest, a number of scientists have tried to approximate the number of lives that could be saved by improving vitamin D intake. Using such associational studies, these scientists have come up with some interesting numbers.

They estimate that if Canadians brought their vitamin D levels up to healthy levels (which I outline in Chapter 2), an estimated 37,000 lives a year would be saved.

Scientists proposed that the following benefits would be achieved:

- ✔ A 25 percent decline in cancer rates
- ✔ A 25 percent decline in heart disease

- ✔ A 60 percent improvement in insulin sensitivity, thus protecting against diabetes
- ✔ Reduction in the risk of multiple sclerosis
- ✔ A 30 percent reduction in the risk of pneumonia
- ✔ A 50 percent reduction in Cesarean sections
- ✔ Complete elimination of rickets and substantial reduction in the rate of osteoporosis

Extrapolating to the United States, which has ten times the population of Canada, more than 300,000 lives a year would be saved by raising vitamin D levels in this country.

Later in the book I discuss just what “healthy” levels of vitamin D might be, and I show you why scientists think that there’s enough evidence to support these numbers.