Vitamin D is a fascinating molecule with a fascinating story. Historically, “vitamins” were defined as chemicals that humans required from their environment that were “vital” to human health. These chemicals were needed only in very small amounts to prevent disease; an absence of a particular vitamin in the diet led to a specific deficiency disease: vitamin C, scurvy; thiamine, beri beri. Other vitamin deficiencies were found to be a bit more complicated: vitamin B12 deficiency was found to cause a type of anemia, dementia, and spinal cord problems.

Because vitamins are required in such small amounts, and are often present in small amounts in foods, their discovery was an opportunity to prevent and cure several diseases. One of these diseases was rickets.

Rickets was common in America and Northern Europe when vitamin D was discovered early in the 20th century. A series of fascinating experiments found that a fat-soluble substance present in cod-liver oil had the ability to prevent and cure rickets. Environmental observations also found that children in the tropics were less likely to develop rickets than those in high northern latitudes, and sunlight seemed to prevent the disease.

This child's bowed legs are typical of rickets
It is nearly impossible to ingest sufficient vitamin D in a typical diet, and it is nearly absent from breast milk. In areas where sunlight is scarce or where culture prevents sun exposure, rickets was more common. Rickets became rare in the U.S. once children’s parents began shoving them full of cod-liver oil, and once vitamin D was added to milk.

Vitamin D is more properly called a “hormone” rather than a vitamin. It’s precursor is naturally produced in the body and is present in the skin in large amounts. When it is exposed to ultraviolet B radiation, as from sunlight, this precursor is converted to another molecule that is absorbed into the blood stream. It travels to the liver where it is converted into a “prohormone” (precursor to a hormone). After leaving the liver, the prohormone can be converted in the kidneys to the hormone form of vitamin D on a (relatively) large scale to be distributed throughout the body, or it can be converted on a small scale in local tissues.

Vitamin D receptors are present in nearly every tissue in the human body. Aside from its effects on bone growth, its various effects are only incompletely understood. But is the prevention of severe vitamin D deficiency such as rickets all we need to know? Growing evidence is suggesting that vitamin D deficiency is more common that previously believed, and that vitamin D may play an important role in many common diseases such as heart disease and cancer.

In the early part of the century, scientists fed rats very limited diets, teasing out the effects of various foods and the micronutrients they contained, including vitamin D. Such controlled experiments are, needless to say, problematic in humans. Rickets was a common, even endemic, disease, and therefore not terribly difficult to study. But other effects of vitamin D may be more subtle. Attempts have been made to correlate other disease states with the relative deficiency in vitamin D that is still common in high latitudes. Part of the difficulty in studying the effects of low vitamin D levels is in simply defining them. Assays that measure vitamin D in the blood are not entirely reliable. Still, we can try to correlate vitamin D levels with obvious deficiency diseases such as rickets, but the environmental studies that look at other possible effects are problematic.

Heart disease is one of our three biggest killers (along with cancer and stroke). One of the better prospective studies done on vitamin D and heart disease followed subjects over time, measuring vitamin D levels and following them to see who developed a first incidence of heart attack. They found that those with low vitamin D levels who also had high blood pressure (a well-recognized risk factor for heart disease) were more likely to develop a first heart attack than hypertensive patients with higher vitamin D levels.

These data are intriguing, but because low vitamin D levels and heart disease are both very common, and because this was not an interventional study, it is difficult to draw firm conclusions, other than more research is probably warranted.

Other studies of the effects of low vitamin D are more problematic. Vitamin D has been convincingly correlated with all-cause mortality, with certain cancers, and with multiple sclerosis. But causation is very difficult to attribute in these cases. Vitamin D deficiency
is common in people with poor diets (including obese people) and in people who are relatively inactive. These are independent risk factors for mortality, heart disease, and some cancers. And while some cellular mechanisms have been discovered that may lend plausibility to a vitamin D hypothesis, there are as of yet no convincing data that allow us to draw conclusions about vitamin D and these diseases.

Low vitamin D levels are quite common, and it is nearly impossible to attain adequate levels with diet alone. We know that vitamin D is necessary to prevent rickets, and that, combined with calcium, it is needed to prevent osteoporosis. We do know that sun exposure will ensure an adequate level of vitamin D and because of a clever regulatory mechanism, will never result in excess vitamin D. But we do not know what a “safe” level of sun exposure is. We know that the relationship between sun exposure, photoaging of the skin, and skin cancers is dose-dependent, but we don’t know where to place the fulcrum in balancing the need for vitamin D and the risk of cancer.

Supplementation is effective in raising vitamin D levels, but we do not yet know what an “optimum” level of vitamin D is, and we don’t know what the long-term effects of supplementation may be. Other fat soluble vitamins have been found to actually increase the risk of cancer if supplemented too aggressively.

The vitamin D story is fascinating, and despite over a century of study, it is still playing out. While we can draw some pretty safe conclusions about the prevention and treatment of some common bone diseases, it is too early to form any useful conclusions about other diseases such as cancer, influenza, or multiple sclerosis. Given our limed knowledge, recommendations on screening and treatment for vitamin D deficiency in reasonably healthy people are neither clear nor final. We have a set of plausible and interesting hypotheses to work with, and now we need some randomized controlled trials to give us data we can really use.

Selected References


