Possible roles for vitamin D in selected infections—TB, colds and flu, HIV, hepatitis C virus and bacterial vaginosis

Lab experiments with cells of the immune system—monocytes and macrophages—have found that these cells produce an enzyme that converts vitamin D into its active form. This suggests that these cells use vitamin D as part of the process of fighting infections and possibly tumors. Other experiments have found that exposure to vitamin D₃ stimulates macrophages to release small molecules that can attack germs.

**Tuberculosis (TB)**

Before potent antibiotics were available, physicians encouraged people with TB to get exposure to sunlight and in some cases vitamin D supplements were administered. However, well-designed clinical trials in the 21st century have found that vitamin D supplements in addition to antibiotics do not confer a major increase in survival or recovery from TB compared to antibiotics alone. Some researchers have suggested that instead of being used as part of treatment, perhaps vitamin D supplements might be more useful in helping to prevent infection with TB. Clinical trials to test this idea have not been done.

**Colds and flu**

Cells lining the lungs can produce high levels of enzymes that convert vitamin D into its active form, vitamin D₃. This finding suggests that these cells may use vitamin D as part of their defense system against infections. Indeed, in laboratory experiments when these cells are treated with vitamin D₃, they also produce small molecules that help protect cells from infection by viruses and bacteria.

Several clinical trials that have tested vitamin D₃ to assess its ability to reduce the risk of developing respiratory tract infections—the common cold and flu—have had mixed results. It is therefore difficult to draw firm conclusions about the role of vitamin D in preventing respiratory infections. Part of the problem arises from issues related to different study designs and methodology.

**HIV**

Observational studies have found that HIV-positive people usually have less-than-ideal levels of vitamin D in the blood and, in some cases, deficiency. Vitamin D deficiency in the setting of HIV infection even occurs in sunny tropical countries. Researchers are not certain why this is the case. One possible explanation is that HIV infection triggers ongoing inflammation in the immune system. By inciting the immune system to overproduce inflammation-related chemical signals or cytokines, it is possible that HIV infection indirectly speeds up enzymes that convert vitamin D₃ into inactive forms.

Supplementation with large amounts of vitamin D does not increase HIV replication in people who are taking ART. Results from two clinical trials suggest that vitamin D₃ does not affect CD4+ cell counts in HIV-positive adults and children.

Larger observational studies have found that vitamin D deficiency has been linked to an increased risk of death among HIV-negative people, particularly from cardiovascular disease. A recent European study with about 2,000 participants has found an association between low vitamin D levels and reduced survival among HIV-positive people. Details about this study appear in *TreatmentUpdate 181*. As the study is observational in nature, it cannot prove that low vitamin D levels are the cause of death. However, the same European researchers are also conducting a large study of vitamin D supplementation, hoping to improve survival rates in HIV-positive people. Interim results
from this study of supplementation should be available in several years.

Researchers have found associations between low levels of vitamin D and pre-diabetes or diabetes in HIV-positive people in several studies. However, it is not clear if vitamin D deficiency led to problems with insulin and blood sugar. Clinical trials are needed to understand the relationship between vitamin D supplementation and pre-diabetes or diabetes in HIV-positive people.

**Hepatitis C virus (HCV)—antiviral and other effects**

Researchers in Israel have performed laboratory experiments with vitamin D, liver cells and HCV. In these experiments, treating HCV-infected cells with vitamin D$_3$ reduced their production of this virus, likely by stimulating the release of interferon. Treating these cells with low concentrations of both vitamin D$_3$ and interferon-alpha also reduced HCV production.

Note that lab experiments with cells and viruses do not reproduce the complexity of an organ or system. These experiments are an interesting first step on the path to conducting further experiments with vitamin D$_3$ and HCV-infected cells. Hopefully they will eventually lead to clinical trials.

Studies with HCV-infected people suggest that some of those with vitamin D deficiency are less likely to respond to HCV therapy than people with higher concentrations of vitamin D in their blood. Also, vitamin D is associated with a reduced risk of rejecting transplanted liver. Vitamin D is also associated with reduced liver inflammation in HCV infection. Unfortunately, due to the observational nature of these studies, firm conclusions about vitamin D’s effects cannot be drawn at this time. Such findings need to be confirmed in robustly designed clinical trials so that the role of vitamin D in HCV infection can be better understood.

**Bacterial vaginosis**

The vagina normally contains a mix of mostly good bacteria and small amounts of bad bacteria. Sometimes women develop an imbalance in the bacteria that live in their vagina, whereby the proportion of bad bacteria increases—bacterial vaginosis (BV). In cases of BV, women can experience such symptoms as itching, burning, pain and discharge, while in some cases BV can occur without causing symptoms. BV does not normally cause serious complications, however, it can do so in cases where the woman is pregnant. BV can increase the risk for HIV transmission and the risk for becoming infected with STIs.

Observational studies have found an association between BV in pregnant, HIV-negative women and vitamin D deficiency. Recently, in a study of 600 non-pregnant women, researchers in the U.S. found an association between BV and vitamin D deficiency among women who were HIV positive. As with so many studies of vitamin D, this was an observational study so it can only find associations and does not prove that vitamin D deficiency causes BV. Indeed, in general, researchers are not certain why some women develop BV, though there are several theories. The present study provides a foundation to conduct more rigorous research to explore this link between BV and vitamin D, particularly among HIV-positive women.

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