Let's make Pakistan D Positive

D Miracle

infomag

2nd-Edition 2019

"Vitamin D is critically important from birth until death. Every cell and tissue in our body has a Vitamin D receptor"

An exclusive interview with Dr. Michael F. Holick on page 3

"Dr. Michael F. Holick"

The Leading Authority on Vitamin D in The World

Miracle
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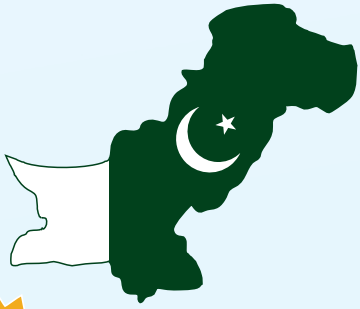
Let's Make PAKISTAN



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Let's Make Pakistan D Positive

Vitamin D deficiency or VDD is a pandemic, yet it is the most under-diagnosed and under treated nutritional deficiency in our country. VDD is widespread in individuals irrespective of their age, gender, race and geography. Vitamin D is photosynthesized in the skin on exposure to UVB rays. Sun exposure alone ought to suffice for Vitamin D sufficiency. However, Vitamin D deficiency is widely prevalent despite plentiful sunshine available mostly in all parts of Pakistan.

Vitamin D deficiency has a bearing not only on skeletal but also on extra-skeletal diseases. Owing to its multifarious implications on health, the epidemic of Vitamin D deficiency in Pakistan is likely to significantly contribute to the enormous burden on its already ailing healthcare system.

Cultural and social taboos often dictate lifestyle patterns such as clothing that may limit sun exposure and a staple diet, which certainly limits Vitamin D rich dietary options. Most Pakistanis struggle for months and years with a number of ailments mainly due to this deficiency despite the fact that Vitamin D supplements are available, yet they are not aware that they need additional Vitamin D.

Our aim of publishing D-Miracle infomag is to impress upon the practicing physicians in our country about the gravity of the Vitamin D deficiency problem throughout Pakistan, so that they may take necessary caution and care in the diagnosis and treatment of Vitamin D deficiency.

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Vitamin D_3 Overview:

Vitamin D is a fat-soluble secosteroid responsible for increasing intestinal absorption of Calcium, Magnesium, Phosphate, and multiple other biological effects. With its pleiotropic actions and health benefits, Vitamin D is regarded to play a key role, not only in bone health, but for the overall health and well being of humans.

Vitamin D that comes from the skin or diet is biologically inert and requires its first hydroxylation in the liver. The vitamin D receptor is present in most tissues and cells in the body exerting a wide range of biological actions, including inhibiting cellular proliferation and inducing terminal differentiation, inhibiting angiogenesis, stimulating insulin production, inhibiting renin production, and stimulating macrophage cathelicidin production. The local production of 1,25(OH)2D may be responsible for regulating up to 2000 genes that may facilitate many of the pleiotropic health benefits that have been reported for Vitamin D.

Common Causes of Vitamin D Deficiency

Obesity

Old Age

Avoiding Sunlight

Location

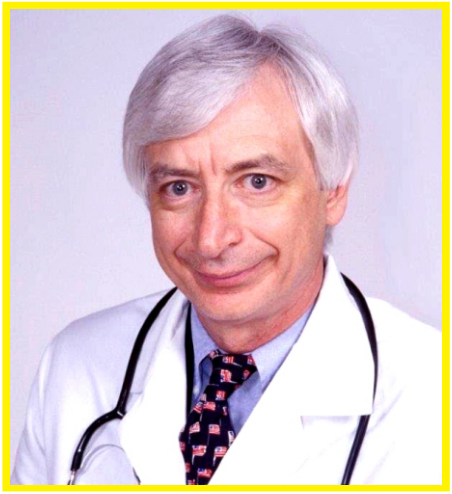
- In cases of obesity, Vitamin D essentially becomes sequestered by fat cells leaving it unavailable for mobilization when needed.
- Older people have thinner skin than younger people and this may mean that they can't produce as much Vitamin D.
- Avoiding sunlight or the use of sun block, both reduce the natural production of Vitamin D.
- Indoor lifestyle reduces production of Vitamin D in human body.

Let's Talk Vitamin D with the leading authority Dr. Michael F. Holick

by Dr. Syeda Saba Aslam
Scotmann Pharmaceuticals

Dated: April 2019

Michael F. Holick, Ph.D., M.D. is a Professor of Medicine, Physiology and Biophysics; Director of the General Clinical Research Unit; and the Director of the Bone Health Care Clinic; and the Director of the Heliotherapy, Light, and Skin Research Center at Boston University Medical Center. As a graduate student he was the first to identify the major circulating form of Vitamin D in human blood as 25-hydroxyvitamin D3. He then isolated and identified the active form of Vitamin D as 1, 25-dihydroxyvitamin D3. He determined the mechanism of how Vitamin D is synthesized in the skin, demonstrated the effects of aging, obesity, latitude, seasonal change, sunscreen use, skin pigmentation, and clothing on this vital cutaneous process. He is the recipient of numerous awards and honors. He has written more than 400 peer reviewed articles, edited or wrote 12 books including "The Vitamin D Solution" and is the recipient of numerous awards including the American Skin Association's Psoriasis Research Achievement Award, the American College of Nutrition Award, the Robert H. Herman Memorial Award, the Linus Pauling Prize in Human Nutrition and many other awards.



Dr. Michael F. Holick
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Professor of Medicine, Physiology and Biophysics,
Director of the General Clinical Research Unit,
Boston University Medical Center.

Dr. Saba: Welcome Dr. Holick and a very good morning to you.

Dr. Michael: It's a pleasure to be here.

Dr. Saba: We would like to start with, why Vitamin D? Why not any other Vitamin or any other…. What brought you into this?

Dr. Michael: When you think about Vitamin D, what's really quite remarkable is that Vitamin D is probably the oldest hormone on the planet. We can show that more than 500 million years ago, some of the earliest life forms exposed to sunlight were making Vitamin D. So, I think that Vitamin D has evolved over these hundreds of millions of years. It plays a very important role, not only for bone health but for overall health and well-being.

Dr. Saba: Sir, which diseases do you think it has the most impact on?

Dr. Michael: When I am most asked this question, what I think is that Vitamin D is critically important from birth until death. Right. So, during pregnancy, Vitamin D, I think plays a very important role for pregnant women. Studies have shown that if you are Vitamin D deficient during pregnancy, you have a higher risk for pre-eclampsia, higher risk for premature births, higher risk for the infant developing wheezing disorders early in life, and higher risk of that infant having dental caries early in life. So, during pregnancy, Vitamin D is very important for both the mom and for the developing infant. We think that during childhood, Vitamin D plays a critical role in reducing the risk of many chronic illnesses later in life. A good study that was done in Finland back in the 1960s, they gave infants, during their first year of life, 2000 units of Vitamin D a day and then they followed them for 31 years. Then they looked at their risk for Type 1 Diabetes and reported and 88% reduced risk of developing type 1 diabetes just by giving the infant 2000 units if Vitamin D during the first year of life. Moreover, there is good evidence that during the first ten years of your life, if you are Vitamin D sufficient, you are more likely not to develop Multiple Sclerosis later in life. There

"Vitamin D is critically important from birth until death"

is evidence that if you live below about 35 degrees latitude for the first ten years of your life, then you have a 50% lower risk of developing Multiple Sclerosis compared to those living above 35 degrees North and South latitude. During young adulthood, we think it is very important for helping to maintain bone health. Often young adults are complaining of aches and pains in their bones and muscles and often their diagnosis is Fibromyalgia. So, pressing on bones, for example, what we call a trigger point, causes pain. That's a classic sign for Vitamin D deficiency- Osteomalacia. So many of these young adults that I see in my clinic, basically they tell me I have given them their lives back because I put them on Vitamin D and many of these aches and pains have resolved. We also have good evidence that it reduces the risk for Breast Cancer. From the Nurses Health Study, they showed that the nurses who had the highest intake of Vitamin D had their blood levels on average of about 48 nanograms per ml. That would be equivalent to taking 3000-4000 units of Vitamin D a day, reducing risk of Breast Cancer by about 50%. Right. Then there are these other pieces of evidence that suggest that it reduces risk of Type 2 Diabetes, neurocognitive dysfunction, depression, and Alzheimer's disease. So, Vitamin D is incredibly important. When you think about this, how is it possible that this Vitamin has so many biological effects. The main reason is that every cell and tissue in your body has a Vitamin D receptor. We have shown and others have shown the same that Vitamin D can influence as much as 2000 genes in your body, by up and down regulation of various activities.

Dr. Saba: So you talked about pregnancy, you talked about Multiple Sclerosis, osteomalacia and also the risk of developing Type 1 Diabetes Mellitus. Sir coming to the genes, you mentioned genes right now. What is the role of Vitamin D on DNA?

Dr. Michael: There is some evidence that Vitamin D sufficiency can remarkably reduce the risk for mortality and mainly cardiovascular mortality. There are also some studies that show that Vitamin D, through its activation in the brain, can help prevent some of these amyloid plaques from developing. And maybe that's one of the reasons why its been related to reducing risk for Alzheimer's disease and also there is some evidence

that Telomerase activity is changed. And as a result, it may actually prolong life as well. So, there are a variety of different activities on DNA. We did a study on healthy adults and asked a simple question. If you give 2000 units of Vitamin D a day, just for a few months and get their White Blood Cells and look at gene expression analysis of about 23000 genes, we were able to show up and down regulation of more than 900 genes in the immune system. We just completed a study where we had given 10000 units of Vitamin D a day for 6 months in healthy adults and we showed up to 2000 genes affecting your immune system and a whole host of other

"Every cell and tissue in your body has a Vitamin D receptor"

biological processes. So Vitamin D does, I think, play a very important role in regulating DNA activity and gene expression.

Dr. Saba: Sir you mentioned about Telomerase. Can you shed some light on that?

Dr. Michael: Right. So, there has been only one study that has been done but that one study did suggest that it may very well have an effect on Telomerase activity. And therefore, decrease the breakdown of Telomeres and therefore prolong life.

Dr. Saba: Sir, can you share with us, what is Telomere and the role of it in the aging process- I have read.

Dr. Michael: Right. So, the concept is that these Telomeres are pieces on your DNA and that you start off with a very long chain of them and then they start to decrease as cells continuously are multiplying and dividing and when they get to a shorter length, then you are at more risk for mortality. And so, if you are able to maintain Telomere length, is that you can improve longevity.

Dr. Saba: Telomeres- a very exciting new topic for Vitamin D I think.
So, where do you see the future of Vitamin D?

Dr. Michael: As you know, the recent study in the New Journal of Medicine, the Vital Study, suggested that may be Vitamin D isn't gonna have much effect on your cardiovascular health for reducing the risk of cancer. But if you read that study carefully, many of them, more than 50% of the subjects were already Vitamin D sufficient and they were now getting 2000 units of Vitamin D a day and so the fact that they didn't see very much of an effect, in my opinion, was not a surprise. But what was really important , what I think about that study, that is not really thought about very carefully, is that there was a 25% statistically significant reduction in cancer mortality. So the patients that had Cancer, who were taking Vitamin D had 25% reduced risk for mortality. So we think that this is very important. I think that Vitamin D is going to continue to make very significant inroads into understanding its overall health benefits. There continues to be probably a dozen or more publications a month, talking about health benefits of Vitamin D. But even now there are some skeptics out there and the issue of how much Vitamin D do you need. A piece of evidence to suggest how much Vitamin D you need for health comes from a

"3000-4000 units of Vitamin D a day, reduces risk of Breast Cancer by about 50%. It reduces risk of Type 2 Diabetes, neurocognitive dysfunction, depression, Alzheimer's disease. "

study by Dr. Hollis and Wagner and they asked a very simple question, which is that we've always known that human breast milk essentially contains little Vitamin D.

So if you give your infant human breast milk as the sole source of nutrition then your infant will be Vitamin D deficient for that period of time. But it makes no sense again from an evolutionary perspective that human milk shouldn't have enough Vitamin D to satisfy their infant's requirement. So they did a study and they showed that if you give lactating women 6000 units of Vitamin D a day, you put enough Vitamin D in her milk to satisfy her infant's requirements. From an evolution perspective, we have probably adapted to the requirement that we all need at least 2000 units of Vitamin D a day. I personally take 6000 units every day. Almost all of my patients are on 3000-5000 units of Vitamin D a day and they are doing great.

Dr. Saba: Sir, coming to dosing. Many people have the concern of toxicity with Vitamin D? What is your take on that?

Dr. Michael: All of us at medical schools have been taught that Vitamin D is one of the most toxic fat-soluble vitamins and to be very careful especially for infants but it turns out that it is not correct. The reason is that Vitamin D toxicity is one of the rarest medical conditions of the world. You literally have to take 50,000 to 100,000 units of Vitamin D a day for like a year before you have to even begin to worry about toxicity. The Endocrine Society practice guidelines after reviewing the literature concluded that you will not see Vitamin D intoxication until your blood level of 25 dihydroxyvitamin D is over 150 nanograms per ml. And if you are Vitamin D toxic, the Calcium is going up and the Phosphate is going up and the parathyroid hormone goes down. And then yes it can lead to nephrocalcinosis, soft tissue calcification, but again its extremely extremely rare. The only time you have to be concerned about Vitamin D toxicity for a physiologic dose of Vitamin D, is if you have Sarcoidosis or Tuberculosis or any type of granulomatous disorder because they are associated with a hypersensitivity to Vitamin D because of the macrophages activating Vitamin D directly.

Dr. Saba: Which one do you think is more important for bone health: Calcium or Vitamin D?

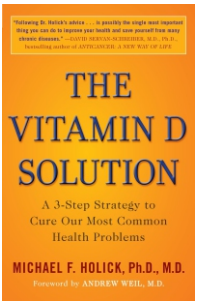
Dr. Michael: You need them both. I mean, there's no question. I mean there are many places in the world, Bangladesh, in Africa where Rickets in children is common even though they have a normal blood level of 25 hydroxyvitamin D. It is because of their severe Calcium deficiency. So, Vitamin D plays a role in increasing intestinal Calcium absorption and then if you have an adequate Calcium and phosphate product, you can then properly mineralize the bone. So I tell all my patients that you need an adequate amount of Calcium preferably from dietary resources if you can. And dairy, in my opinion, is an excellent source along with adequate Vitamin D. So they go hand in hand.

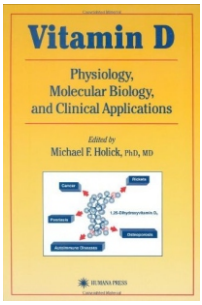
Dr. Saba: So Calcium and Vitamin D go hand in hand.

Thank you Sir. That was a really enlightening talk with you and I hope my viewers have also learned a lot from you.

Dr. Michael: Thank you.

Dr. Holick's Publications





Vitamin D_3
(Cholecalciferol)
& Bone Health

Vitamin D plays an essential role in maintaining a healthy mineralized skeleton for most land vertebrates including humans. Vitamin D insufficiency and Vitamin D deficiency is now being recognized as a major cause of metabolic bone disease in the elderly. It is generally accepted that an increase in Calcium intake to 1000-1500 mg/d along with an adequate source of Vitamin D of at least 400 lU/d is important for maintaining good bone health. It is well known that Vitamin D deficiency is associated with rickets in children and osteomalacia in adults (Holick, 1994).

Before the epiphyseal plates close, Vitamin D deficiency causes a disorganization and hypertrophy of the chondrocytes at the mineralization front as well as a mineralization defect, resulting in the short stature and bony deformities that are characteristic of Vitamin D deficiency rickets. Osteomalacia, on the other hand, occurs after the epiphyseal plates close; therefore, this disease of adults is more subtle. There is a mineralization defect in the skeleton resulting in poor mineralization of the collagen matrix (Holick 1994). Although this does not cause bony deformities, it can cause severe osteopenia (a decrease in the opacity of the skeleton as seen by x-ray) that results in increased risk of skeletal fractures. In addition, some patients with osteomalacia complain of localized or generalized unrelenting deep bone pain.

Osteoblasts, which are responsible for laying down the collagen and protein matrix in the skeleton, possess receptors for Vitamin D (VDR). 1,25(OH)2D3 stimulates the synthesis of noncollagenous proteins such as osteocalcin, osteopontin and osteonectin, increases alkaline phosphatase activity and decreases collagen synthesis. There are several studies to support the hypothesis that the principal function of Vitamin D in mineralizing bone is through its action on maintaining an adequate calcium X phosphorus product in the circulation and extracellular fluid space.

Supplementation of Vitamin D for maintaining a healthy mineralized skeleton is to ensure that the blood and extracellular concentrations of Calcium and Phosphorus are adequate for the deposition of Calcium hydroxyapatite in the bone matrix that had been laid down by the osteoblasts.

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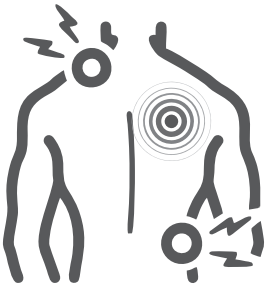
Vitamin D_3

(Cholecalciferol)

& Aches and Pains



Low Vitamin D levels are implicated in various chronic pain conditions. Research has shown that Vitamin D exerts anatomic, hormonal, neurological, and immunological influences on pain manifestation, thereby playing a role in the aetiology and maintenance of chronic pain states and associated comorbidity.

Persistent pain is associated with Vitamin D-related bone demineralization, myopathy, and musculoskeletal pain. Pain pathways associated with cortical, immunological, hormonal, and neuronal changes are potentially also influenced by Vitamin D levels.

Vitamin D levels have been found to be low in certain groups of patients with various pain states. Vitamin D deficiency has been associated with headache, abdominal, knee, and back pain, persistent musculoskeletal pain, costochondritic chest pain, failed back syndrome and with fibromyalgia.

Long-term Vitamin D deficiencies have been linked to a weakened immune system and to chronic inflammation. Chronic inflammation, in turn, leads to debilitating health conditions; many of these are characterised by pain as the disabling symptom. Serum Vitamin D deficiency [25(OH)D] is considered a risk factor for Type 1 Diabetes, Multiple Sclerosis, and especially Autoimmune Rheumatic Diseases (ARD). The severity of Systemic Lupus Erythematosus and Rheumatoid Arthritis has been associated with serum Vitamin D deficiency. Vitamin D deficiency has been linked to other diseases that present with pain as a symptom. Cystic fibrosis patients experience chronic pain in a variety of sites (head, sinuses, back, and chest). Individuals with cystic fibrosis are at risk of Vitamin D deficiency due to limited sun exposure and malabsorption. Low bone density and osteopaenia appear to contribute to chronic pain in cystic fibrosis patients and are potentially related to low 25(OH)2D3 levels. Individuals suffering from chronic pain usually experience other comorbidities such as sleep, anxiety, and mood disorders.

In conclusion, significant improvements in assessment of sleep, pain levels, well-being, and various aspects of quality of life with Vitamin D supplementation have been shown.

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Vitamin D3
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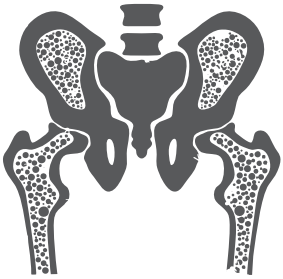
& Osteoporosis



Fractures due to osteoporosis often occur in the hip, wrist or spine and can lead to considerable disability or even death. Those who survive often have reduced mobility and may require greater social and nursing care. Vitamin D is necessary for building strong bone. Older people often have low Vitamin D levels because of a lack of exposure to sunlight and low consumption of Vitamin D in their diet. Therefore, it has been suggested that taking additional Vitamin D in the form of supplements may help to reduce the risk of fractures of the hip and other bones. A study showed that Vitamin D Receptor (VDR) ApaI polymorphism significantly decreased the osteoporosis risk in postmenopausal women. In Asian populations, VDR BsmI and VDR FokI were associated with an increased risk of Post-Menopausal Osteoporosis (PMOP).

Another large study included 31,022 participants (mean age, 76 years; 91% women) with 1111 incident hip fractures and 3770 nonvertebral fractures. Benefits at the highest level of Vitamin D intake were fairly consistent across subgroups defined by age group, type of dwelling, baseline 25-hydroxyvitamin D level, and additional Calcium intake. It was concluded that high-dose Vitamin D supplementation was favorable in the prevention of hip fracture and any nonvertebral fracture in persons 65 years of age or older.

Several osteoporosis treatment guidelines by US Endocrinology groups including the American Association of Clinical Endocrinologists and American College of Endocrinology Clinical Practice Guidelines for the diagnosis and treatment of postmenopausal osteoporosis insist on the correction of Vitamin D deficiency after the evaluation of Secondary Osteoporosis. Another study revealed that the incidence of hip fractures was reduced by 30 percent with the use of Vitamin D supplementation.

Another Cochrane review found that Calcium and Vitamin D are effective at preventing and treating corticosteroid-induced bone loss at the lumbar spine and forearm. The treatment appears to be safe.

Therefore, it has been suggested that taking additional Vitamin D in the form of supplements may help to reduce the risk of fractures of the hip and other bones.

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Vitamin D_3

(Cholecalciferol)

In Winter

The major source of Vitamin D in humans is ultraviolet B (UVB)-induced dermal synthesis of cholecalciferol, whereas food sources are believed to play a lesser role. Mean serum 25-hydroxyvitamin D [25(OH)D] concentrations in humans vary significantly with the seasons. High serum concentrations in the summer and low concentrations in the winter have been observed in young and old persons, reflecting the amount of exposure to the sun. Thus, because the dietary sources of Vitamin D are scarce, a low Vitamin D status might be expected during the winter months. A study in the early 1980s showed that during the winter, 20 of 85 (23.5%) 11–17-y-old Finnish adolescents had serum 25(OH)D concentrations <12.5 nmol/L. In addition, a recent study by Lehtonen-Veromaa et al showed that 25 of 185 (13.4%) 9–15-y-old girls had serum 25(OH)D concentrations <20 nmol/L in the winter.

Mild vitamin D deficiency leads to secondary hyperparathyroidism in postmenopausal women and in the elderly, which has negative effects on Calcium and bone metabolism. In these groups, low serum 25(OH)D and elevated serum intact parathyroid hormone (iPTH) concentrations are associated with low bone mineral density. In addition, increased Vitamin D intake was shown to suppress the seasonal variations of serum 25(OH)D and iPTH concentrations in the elderly.

Studies by Ala-Houhala et. al and Lamberg-Allardt et al showed that serum 25(OH)D concentrations are significantly lower in 11–17-y-old adolescents than in children <10 y of age. Regardless of the mean serum 25(OH)D concentrations being within the normal range, the study showed that a low Vitamin D status is common among adolescents during the winter season; an average of 14% of the females had serum 25(OH)D concentrations <25 nmol/L.

Thus, the studies indicate that a large percentage of adolescents have low Vitamin D status during the winter and that the cutoff generally used for adequate serum 25(OH)D concentrations (>25 nmol/L) is too low to maintain an appropriate serum iPTH concentration during the winter.

Moreover, the high prevalence of maternal hypovitaminosis D during winter months may have detrimental effects on fetal skeletal growth also.

In conclusion, increasing the Vitamin D intake can ameliorate the impact of low UVB availability on serum 25(OH)D status during winters.

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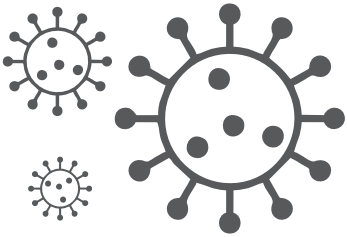
Vitamin D_3

(Cholecalciferol)

& Viral Infections



The possible interactions between viral infections and Vitamin D appear to be more complex than previously thought. Some recent 2019 findings indicate a complex interplay between viral infections and Vitamin D, including

- the induction of anti-viral state,
- functional immunoregulatory features,
- interaction with cellular and viral factors,
- induction of autophagy and apoptosis and
- genetic and epigenetic alterations.

While crosstalk between Vitamin D and intracellular signaling pathways may provide an essential modulatory effect on viral gene transcription, the immunomodulatory effect of Vitamin D on viral infections appears to be transient. Mounting research suggests Vitamin D deficiency may actually be a major cause of influenza. People with the lowest Vitamin D levels report having significantly more colds or cases of flu. Scientific review confirms Vitamin D optimization boosts immunity and cuts rates of cold and flu. Among people with Vitamin D blood levels below 10 ng/mL, taking a supplement cuts risk of respiratory infection by 50 percent. A recent study published in October 2018 revealed that severe hand, foot, and mouth virus is 2.9 X more likely if Vitamin D receptors are poor.

Low serum levels of Vitamin D are associated with increased hepatitis B virus (HBV) replication. Many studies indicate that VDR expression is downregulated in HBV-transfected cells, thereby preventing Vitamin D from inhibiting transcription and translation of HBV in vitro. Yousif et. al demonstrated that lower 25(OH)D levels were associated with HE and SBP in cirrhotic patients. In addition, it may be considered a prognostic parameter for the severity of liver cirrhosis.

Recent data suggest a key role of Vitamin D in the control of inflammatory cytokine responses during Dengue Virus infection of human macrophages via the TLR4/NF-B/miR-155-5p/SOCS-1 axis. Another 2019 study showed that 25-hydroxyvitamin D attenuated rhinovirus-induced expression of ICAM-1 and PTAFR in a respiratory epithelial cell line. The findings suggest possible mechanisms by which Vitamin D may enhance resistance to rhinovirus infection and reduce the risk of secondary bacterial infection in Vitamin D-deficient individuals.

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Vitamin D_3

(Cholecalciferol)

& Type-I Diabetes

Type 1 Diabetes is characterized by autoimmune destruction of insulin-producing beta cells in the pancreas. By the time Type 1 Diabetes is diagnosed, about 80% of the beta cells have been destroyed. One of the environmental factors thought to be protective against the development of Type I Diabetes, is early supplementation with Vitamin D. Epidemiological studies suggest that supplementation with Vitamin D in infants might be important in conferring protection against the development of Type 1 Diabetes.

Studies suggest that Vitamin D supplementation in infancy may offer protection against the development of Type 1 Diabetes. Meta-analysis of data from four studies, which included children from many different countries, indicated that children being supplemented had a 29% reduction in risk of developing Type 1 Diabetes compared with their peers who were not being supplemented.

The reduction in risk was also demonstrated in a cohort study. Furthermore, there is evidence of a dose-response effect. A cohort study showed that those who had rickets diagnosed earlier in life (and were thus more likely to be those with the lowest amounts of Vitamin D) were more likely to develop Type 1 Diabetes. In addition, those that were supplemented more regularly or had higher doses of Vitamin D supplements, displayed a reduced risk of developing Type 1 Diabetes. The positive findings with increasing frequency of use were also confirmed in case-control studies that looked at this variable.

The exact mechanism by which Vitamin D supplementation protects against Type 1 Diabetes is unclear, but it has been suggested that this is likely to be through the prevention of hypovitaminosis D. The identification of receptors for the active form of Vitamin D in both β cells and immune cells has led to a number of studies for the delineation of these pathways. There is evidence for a physiological role for Vitamin D in the immune system, and also for a protective effect of the Vitamin from cytokine-induced β cell dysfunction.

In conclusion, there is evidence from observational studies that Vitamin D supplementation in infancy might be protective against the development of Type 1 Diabetes. Despite limitations, the Hill criteria for causality seem to be fulfilled by many meta analyses.

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Vitamin D3
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& Type-II Diabetes

Type 2 Diabetes has become a significant global health care problem. Type 2 Diabetes is associated with serious morbidity and increased mortality. Although therapies for Type 2 Diabetes and its complications have improved over the last few decades, the increasing burden of Type 2 Diabetes highlights the need for innovative approaches for the prevention and management of the disease.

There is mounting evidence suggesting that Vitamin D may influence several non-skeletal medical conditions, including cardiovascular disease, cancer, autoimmune disorders and Type 2 Diabetes. A potential role of Vitamin D in Type 2 Diabetes is suggested by a reported seasonal variation in the control of glycemia in patients with Type 2 Diabetes, being worse in the winter when hypovitaminosis D is more prevalent (Campbell et al., 1975). Additional evidence for a role of Vitamin D in Type 2 Diabetes comes from a large number of cross-sectional studies, which have generally reported an inverse association between Vitamin D status and prevalent hyperglycemia. Recently, longitudinal observational studies and intervention studies have also been published on the relationship between Vitamin D and Type 2 Diabetes. Many observational longitudinal studies have shown an inverse association between the Vitamin D status (25(OH)D or self-reported Vitamin D intake) and the development of Type 2 Diabetes.

From a biological perspective, the presence of the Vitamin D receptor in many cell types and organs, and the local production of 1, 25(OH)2D in several extrarenal organs, including β-pancreatic cells, supports potential broad-ranging effects of Vitamin D outside of skeletal health, including Type 2 Diabetes. Vitamin D is thought to have both direct (by the activation of the Vitamin D receptor) and indirect (by the regulation of calcium homeostasis) effects on various mechanisms related to the pathophysiology of Type 2 Diabetes, including impaired pancreatic-β cell function and insulin resistance (Pittas et al., 2007b).

Several possible reasons may account for the attenuation of the association between Vitamin D and Type 2 Diabetes seen in observational studies and published RCTs.

In conclusion, there is a biological plausibility of an important role of Vitamin D in Type 2 Diabetes, and lower Vitamin D status and intake are associated with higher risk of incident Type 2 Diabetes in observational studies.

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Vitamin D_3

(Cholecalciferol)

& Heart

Heart failure is a major health problem in our society. Clinical studies demonstrated that a low Vitamin D status is prevalent in patients with Heart Failure (HF). Several studies have already proved an association between Vitamin D deficiency and a poor outcome in patients with HF and reduced ejection fraction. Vitamin D suppresses activation of the cardiac renin–angiotensin system and of the natriuretic peptides, regulates the extracellular matrix turnover, Calcium flux, and myocardial contractility. It also affects the differentiation and proliferation of cardiomyocytes, which may mediate antihypertrophic and antihypertensive effects of Vitamin D and protect against myocardial dysfunction.

Other studies showed a lack of Vitamin D to be associated with increased cardiovascular risk and various diseases, including hypertension, diabetes, obesity, vascular inflammation, left ventricular (LV) hypertrophy, and Congestive Heart Failure (CHF).

A similar study by Zitterman et al. investigated the association between the Vitamin D metabolite Calcitriol and the prognosis in 383 end-stage congestive HF patients with an LVEF below 35%. There was a high prevalence of low calcitriol [1,25(OH)2D] levels, and deficient calcitriol levels were associated with poor clinical outcome in these patients. Gotsman et al. demonstrated that Vitamin D deficiency [25(OH)D <10 ng/mL] had a higher prevalence in patients with HF compared with the control group (28% vs. 22%) and was a significant predictor of reduced survival. 75% of those HF patients had an Ischaemic Heart Disease (IHD), but there was no differentiation relating to LVEF. Pilz et al. reported in the framework of the LURIC study that in patients who were routinely referred to coronary angiography, low levels of 25(OH)D (severe deficiency <10 ng/mL, moderate deficiency 10–20 ng/mL, and insufficiency 20–30 ng/mL) and 1,25(OH)2D were associated with HF, deaths due to HF and sudden cardiac death.

The Framingham Heart Study showed that Vitamin D status is strongly associated with variation in subcutaneous and especially visceral adiposity.

To conclude, several studies elicit the significance of Vitamin D as a marker for diagnosis and therapy of cardiovascular diseases. Studies reported that vitamin D therapy is relatively easy, cheap, and safe for the prevention and better prognosis of cardiovascular diseases.

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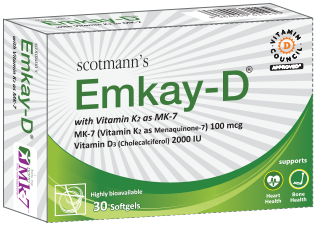

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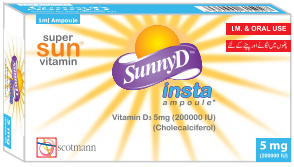

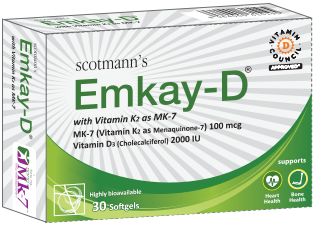

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Vitamin D3
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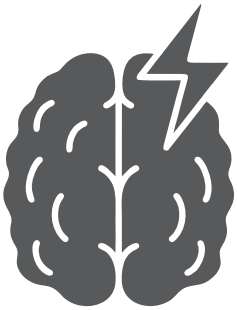
& Stroke



Vitamin D insufficiency is common in acute stroke patients, may precede admission, and is highly prevalent in the years after stroke as sun exposure and dietary Vitamin D decline. It has been suggested that the relevant risk factor for stroke associated with 25(OH)D insufficiency in hypertension is attributable to compensatory secondary hyperparathyroidism.

It has also been shown that low levels of 25-hydroxy Vitamin D [25(OH)D] and 1,25-dihydroxyvitamin D [1,25(OH)2D] are independent predictors of total mortality in patients scheduled for coronary angiography who were participating in the Ludwigshafen Risk and Cardiovascular Health (LURIC) study. In cross-sectional analyses, hemiplegic patients with acute stroke showed significantly reduced 25(OH)D concentrations compared with healthy controls. Data from a population-based study showed that elderly persons with a low intake of Vitamin D and low serum concentrations of 1,25(OH)2D were at increased risk for future strokes even after adjustment for age, sex, smoking, and functional capacity.

In a cohort of >3000 patients referred to coronary angiography, low levels of 25(OH)D and 1,25(OH)2D were independent predictors for fatal stroke and were reduced in patients with a history of previous CVD events at baseline. In particular, patients after acute stroke are at increased risk for Vitamin D insufficiency due to reduced sun exposure and low dietary intake. Vitamin D supplementation in stroke patients has already been shown to reduce osteopenia, fractures, and falls while improving muscle strength. Apart from these beneficial effects, results suggest that Vitamin D might also directly protect against stroke. This hypothesis is supported by data indicating that Vitamin D may protect against hypertension, diabetes mellitus, and atherosclerosis.

With reference to the above studies and the meta-analysis that found an increased survival in persons treated with Vitamin D, researchers are of the opinion that it is a promising and safe preventive/therapeutic approach to supplement Vitamin D in patients after stroke and at high risk for stroke to maintain 25(OH)D concentrations of at least 75 nmol/L (30 ng/mL), which have been shown to be most effective in producing favorable health outcomes.

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Vitamin D_3

(Cholecalciferol)

& Cancer

Long prescribed to prevent and treat bone-related disorders, supplemental Vitamin D has been viewed in recent years as a potential strategy for preventing various cancers. Laboratory studies have shown the presence of Vitamin D receptors in many tissues and have suggested plausible Vitamin D pathways that may be related to cancer, and observational studies have shown associations between low serum levels of 25-hydroxyVitamin D and increased risks of various cancers.

It has been previously recognized that mutations in genes involved in response to hormones, their metabolism or actions may affect the prognosis of disease and thus act as modifiers. Correspondingly, 1,25(OH)2D binds to the VDR (a ligand-dependent transcription factor) and polymorphisms in the VDR gene have been shown to modify the activity of this VitD–VDR complex: for example, rs11568820 is situated in the VDR promoter region and can influence transcriptional activity, while rs2228570 affects the translational start site.

Therefore, it is hypothesized that not only Vitamin D status but also expression and structure of VDR determine molecular actions, and can potentially modify cancer risk and survival. The VitD–VDR complex has the ability to exert downstream biological effects; amongst others, it can regulate the expression of multiple target genes, including several with anti-tumour properties. Moreover, polymorphisms in the VDR gene have been linked to cancer risk, including prostate, breast, skin and bowel, and VDR expression has been linked to survival in prostate and breast cancer.

Hepatic stellate cells (HSCs) play critical roles in liver fibrosis and hepatocellular carcinoma (HCC). Vitamin D receptor (VDR) activation in HSCs inhibits liver inflammation and fibrosis. We found that p62/SQSTM1, a protein upregulated in liver parenchymal cells but downregulated in HCC-associated HSCs, negatively controls HSC activation. Total body or HSC-specific p62 ablation potentiates HSCs and enhances inflammation, fibrosis, and HCC progression. Loss of p62 in HSCs impairs the repression of fibrosis and inflammation by VDR agonists. This demonstrates that p62 is a negative regulator of liver inflammation and fibrosis through its ability to promote VDR signaling in HSCs, whose activation supports HCC. In conclusion, recent studies provide the evidence for the potential beneficial role in cancer prevention.

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Vitamin D_3

(Cholecalciferol)

& Breast Cancer

Vitamin D is reported to have anticancer activities against many cancer types, including breast cancer. Reports from epidemiologic and mechanistic studies have demonstrated that Vitamin D inhibits cancer cell proliferation, induces apoptosis, and decreases angiogenesis. There have been a staggering number of studies and more than a dozen meta-analyses which have explored the inverse relationship. A 50% reduction in the risk of breast cancer was observed in most studies if the woman is Vitamin D sufficient, 2X reduction of deaths from Breast Cancer if have enough Vitamin D and a 3x reduction of the chance of having breast cancer.

In patients with a 25(OH)D3 level below 50 nmol/L, higher predicted probabilities of breast cancer have been reported. The results of a pooled analysis of two randomized trials and a prospective cohort study demonstrated that breast cancer risk was markedly lower with a higher circulating 25(OH)D3 level (≥150 nmol/L). Similarly, the result of a meta-analysis showed a protective relationship between circulating 25(OH)D3 level and breast cancer development in premenopausal women. Studies confirm that 25(OH)D3 levels drop considerably further in breast cancer patients on anti-tumor treatment.

A plausible mechanism for chemotherapy-induced vitamin D deficiency has been described in the literature. The anti-neoplastic drugs such as taxol are ligands for the pregnane X receptor (PXR) and thereby enhance the catabolism of 25(OH)D3 and 1,25(OH)2D3. Anticancer chemotherapies are also known to cause gastrointestinal toxicity, which can lead to reduced absorption of Vitamin D from the gut. Thus, Vitamin D deficiency would be expected in almost all breast cancer patients receiving chemotherapy, which could lead to a greater risk of not only bone-health-related problems, but also compromise clinical outcomes of breast cancer treatment.

Estrogen and selective estrogen receptor modulators (SERMs) can modulate 1-alpha-hydroxylase activity in the kidney and facilitate the synthesis of more 1,25(OH)2D3. Therefore, supplementation of Vitamin D is recommended both for the prevention and during treatment of breast cancer.

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Vitamin D_3

(Cholecalciferol)

& Female Infertility

Vitamin D has a biologically plausible role in female reproduction. In human ovarian tissue, 1,25(OH)2D3 stimulated progesterone production by 13%, estradiol production by 9%, and estrone production by 21%. Likewise, it was demonstrated in a choriocarcinoma cell line that P450 aromatase activity and expression are stimulated by calcitriol and that an atypical Vitamin D response element is located in CYP19 (CYP19A1) (encoding P450 aromatase) promoter. 1,25(OH)2D3 regulates human chorionic gonadotropin expression and secretion in human syncytiotrophoblasts and increases placental sex steroid production. Many studies have demonstrated that Calcitriol promotes Calcium transport in the placenta, stimulates placenta lactogen expression, and regulates HOXA10 expression in human endometrial stromal cells. HOXA10 expression is important for the development of the uterus and essential for endometrial development, allowing uterine receptivity to implantation.

In a study among 84 infertile women undergoing IVF, women with higher levels of 25(OH)D in serum and follicular fluid were significantly more likely to achieve clinical pregnancy following IVF and high Vitamin D levels were significantly associated with improved parameters of controlled ovarian hyperstimulation.

Polycystic Ovary Syndrome: PCOS is the most common cause of anovulatory infertility in women. There is some evidence suggesting that Vitamin D deficiency might be involved in the pathogenesis of insulin resistance and the metabolic syndrome in PCOS. In a study among 100 women with PCOS from Turkey, the authors observed a correlation of 25(OH)D levels with testosterone and DHEAS levels and the LH/FSH ratio. Also, Vitamin D deficiency was found to be more common in PCOS women than in controls in an Iranian cohort including 85 PCOS and 115 control women, as well as in a smaller observational study including 52 women (25 PCOS women and 27 controls) from Edinburgh.

The authors found that Vitamin D deficiency was independently associated with lower insulin sensitivity and lower HDL-C levels (independent of BMI and waist-to-hip ratio). Vitamin D may have a beneficial effect on insulin action by stimulating the expression of insulin receptors and thereby enhancing insulin responsiveness for glucose transport. Likewise, Metformin treatment combined with Calcium and Vitamin D supplementation resulted in a higher number of dominant follicles when compared with Metformin alone and placebo, which might indicate a beneficial effect on fertility.

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Vitamin D3
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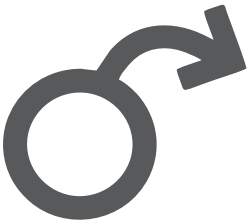
& Male Infertility



Vitamin D might play an important role in the extra testicular maturation of sperm by influencing capacitation and might modulate sperm survival. In a study investigating human sperms at the molecular level, it was found that 1,25(OH)2D3 has an effect on increased sperm survival. More recently, Aquila et al. demonstrated that 1,25(OH)2D3 through VDR increases intracellular Ca2+ levels, motility and acrosin activity revealing an effect of Vitamin D in the acquisition of fertilizing ability in human sperm.

In detail, Blomberg Jensen et al. found a positive correlation of 25(OH)D serum levels with sperm motility and progressive motility. Moreover, men with Vitamin D deficiency (<10ng/ml) had a lower proportion of motile, progressive motile and morphologically normal spermatozoa compared with men with sufficient Vitamin D status (>30ng/ml). They also found that 1,25(OH)2D3 increased intracellular Calcium concentration in human spermatozoa through VDR-mediated Calcium release from intracellular Calcium storage, increased sperm motility and induced the acrosome reaction in vitro. Moreover, Foresta et al. found a significantly lower serum 25(OH)D levels in men with testiculopathy when compared with control subjects.

Results from the European Male Aging Study (EMAS) suggest an independent association of Vitamin D status with compensated as well as secondary hypogonadism. Moreover, previous data indicate that Vitamin D therapy might increase testosterone levels. In detail, men undergoing a weight reduction program received either 83g (3332 IU) Vitamin D daily for 1 year (n=31) or placebo (n=23). Compared with baseline values, a significant increase in total testosterone levels, bioactive testosterone, and free testosterone levels were observed in the Vitamin D supplemented group. By contrast, there was no significant change in androgen levels in the placebo group.

With reference to the findings above, it was concluded that the role of Vitamin D in male fertility should also not be ignored. Vitamin D supplementation can be recommended. The discovery that 1,25(OH)2D3 influences sperm function may be useful for the development of novel therapeutic approaches to the treatment of male reproductive disorders.

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Vitamin D_3

(Cholecalciferol)

& Hyperparathyroidism

Hyperparathyroidism and how it is related to Vitamin D has always been a subject of discussion among medical experts. There are two types of hyperparathyroidism: primary and secondary. Primary hyperparathyroidism is defined as a disorder in the parathyroid glands which means that there is too much secretion of parathyroid hormone (PTH) from one or more overactive, enlarged parathyroid glands.

Secondary hyperparathyroidism is a disorder such as kidney failure that causes the overactivity of parathyroid. The excessive PTH triggers the over secretion of Calcium into the bloodstream. Because of this, the bones may lose a big amount of Calcium but may increase in the urine, causing kidney disorder called kidney stones. PTH can also lower down the levels of blood phosphorus by increasing the phosphorus excretion in the urine. A person diagnosed with hyperparathyroidism may experience subtle symptoms, severe ones, or none at all.

Calcium and Vitamin D supplements are known as the primary treatments for hyperparathyroidism regardless of the cause, with the only difference that arises from the parathyroid hormone's inactivity due to hypomagnesemia. Since parathyroid hormone or PTH is necessary for kidneys to produce an active form of Vitamin D, patients diagnosed with hyperparathyroidism do not have enough PTH; thus, these patients could not naturally produce enough Vitamin D needed to absorb Calcium in the intestines. Thus, it is easy to understand hyperparathyroidism and how it is related to Vitamin D because the two are intertwined.

Vitamin D deficiency exacerbates primary hyperparathyroidism and vice versa. With care, Vitamin D supplementation can safely be given to selected patients with asymptomatic primary hyperparathyroidism and is suggested before deciding on medical or surgical management.

Moreover, monitoring serum Calcium concentration and urinary Calcium excretion is recommended while achieving Vitamin D repletion.

While its cause is unknown, doctors and medical experts use Vitamin D to treat this disease at least as a supplemental treatment. Patients diagnosed with hyperparathyroidism are advised to take supplemental Vitamin D orally.

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Vitamin D_3

(Cholecalciferol)

& Sickle Cell Disease

Sickle cell disease (SCD) is caused by mutations in the beta-hemoglobin gene (HBB). The bone in SCD is affected by microinfarction, osteopenia, osteoporosis, osteomyelitis, and osteonecrosis. Vitamin D and Calcium are required for optimal bone health. Both low 25(OH)D and bone mineral density (BMD) have been described in children with SCD. For clinical endpoints like BMD, fracture risk and adequate dental health, a serum concentration of 25(OH)D greater than 30 ng/ml is recommended. A study showed that 65% of children with SCD had low serum 25(OH)D levels and another study showed that 25(OH)D levels were suboptimal (<20ng/ml) with 64% of patients having a low BMD compared with age, race and sex-matched controls.

While treatment with Vitamin D and Calcium improved both 25(OH)D levels and BMD over 12 months of therapy, long term Vitamin D and Calcium therapy is likely to be required given the chronicity of SCD and its relentless vaso-occlusive, hemolytic and inflammatory complications. Because the low BMD was observed in young adults, a time when bone growth and BMD should be normal, screening for Vitamin D deficiency should be considered at an earlier age, preferably in childhood.

Moreover, in sickle cell disease, respiratory infection and asthma may lead to respiratory complications that are a leading cause of morbidity and mortality. Vitamin D has anti-infective and immunomodulatory effects that may decrease the risk of respiratory infections, asthma, and acute chest syndrome. In pediatric patients with sickle cell disease, 2-year monthly oral Vitamin D3 was associated with a >50% reduction in the rate of respiratory illness during the second year, with similar decreases associated with high- and standard-dose treatment.

In summary, Vitamin D and Calcium supplementation for12 months normalizes 25(OH)D levels and improved BMD in adults with SCD. A useful approach might be to screen young children for Vitamin D deficiency and BMD before generalized bone disease develops and to institute long-term treatment before established bone damage occurs.

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SunnyD™ Vitamin D3 (Cholecalciferol)

Vitamin D3
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& Skin Diseases

There is an intertwined bonding that exists between Vitamin D and skin and it seems only "natural" to incriminate Vitamin D deficiency in a long list of cutaneous disorders including:

Psoriasis: The possible role of Vitamin D deficiency in psoriasis can include the loss of the anti-proliferative function of Vitamin D, the loss of the anti-inflammatory and anti-angiogenic activity of Vitamin D and the unchecked proliferation of Th1 and 17 cells on one hand and unchecked inhibition of Tregs on the other hand.

Acne: A recent study showed that 1,25(OH)2D inhibits P. acnes-induced Th17 differentiation, and sebocytes were identified as 1,25(OH)2D responsive target cells, indicating that Vitamin D analogs may be effective in the treatment of acne.

Hair loss: Vitamin D has been suggested to be necessary to delay the aging phenomena, including hair loss . Recently it has been shown that 1,25(OH)2D/VDR promotes the ability of β-catenin to stimulate hair follicle differentiation.

Vitiligo: Vitamin D protects the epidermal melanin unit and restores melanocyte integrity via several mechanisms including controlling the activation, proliferation, migration of melanocytes and pigmentation pathways by modulating T cell activation, which is apparently correlated with melanocyte disappearance in vitiligo.

Pemphigus Vulgaris and Bullous Pemphigoid: Vitamin D, through its participation in several immune-modulatory functions including B cells apoptosis, Th2 cell differentiation, apoptotic enzyme regulation, and Tregs functions, may be actively involved in the immune regulation of such diseases.

Atopic dermatitis: Studies have suggested that Vitamin D, through various mechanisms including immunomodulation, may alleviate the symptoms of AD. The majority of these studies indicate an inverse relationship between the severity of atopic dermatitis and Vitamin D levels.

On the basis of currently available data, it is clear that supplemental Vitamin D should be the preferred recommendation toward achieving its normal serum levels, thereby avoiding the deleterious effects accompanied by its deficiency.

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& Schizophrenia

The central nervous system is increasingly being recognized as a target organ for Vitamin D via its wide-ranging steroid hormonal effects and via the induction of various proteins such as nerve growth factor. There is now widespread recognition that hypovitaminosis D may contribute to a broad range of adverse health outcomes including neurological and neuropsychiatric disorders. Of particular interest to the hypothesis linking Vitamin D deficiency and schizophrenia, the enzyme required for the production of 1,25(OH)D3 has now been identified in the human brain and there is evidence from rodent models demonstrating that transient prenatal Vitamin D deficiency results in persistent changes in adult brain structure, neurochemistry and behavior.

97% of patients with schizophrenia are Vitamin D deficient. Studies have shown that Schizophrenia is associated with low natal Vitamin D. A meta-analysis showed that Schizophrenia was twice more likely if Vitamin D deficient. The Schizophrenia Bulletin Editorial speculated that Vitamin D could be a major player in Schizophrenia development. Schizophrenia is associated with poor Vitamin D Receptor genes and the risk is decreased if given Vitamin D after birth.

Schizophrenia research is invigorated at present by the recent discovery of several plausible candidate susceptibility genes identified from genetic linkage and gene expression studies of brains from persons with schizophrenia. Low Vitamin D during brain development interacts with susceptibility genes to alter the trajectory of brain development, probably by epigenetic regulation that alters gene expression throughout adult life. Vitamin D is an attractive "environmental" candidate because it appears to explain several key epidemiological features of schizophrenia. Vitamin D is an attractive "genetic" candidate because its nuclear hormone receptor regulates gene expression and nervous system development. The polygenic quality of schizophrenia, with linkage to many genes of small effect, may be brought together via this "Vitamin D hypothesis".

There is also a broader set of environmental and genetic factors interacting via the nuclear hormone receptors to affect the development of the brain leading to schizophrenia.

It is therefore concluded that Vitamin D supplementation during the first year of life is associated with a reduced risk of schizophrenia. Preventing hypovitaminosis D during early life may reduce the incidence of schizophrenia.

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Vitamin D_3 (Cholecalciferol) & Sleep

Sleep disturbances have been associated with poor health indicators and with increased risk of morbidity and mortality. Studies that have compared brain regions associated with sleep-wake cycles and Vitamin D target neurons in the diencephalon and other brainstem nuclei, suggest vitamin D has direct effects on the initiation and maintenance of sleep.

Comparisons of brain regions associated with sleep–wake regulation and Vitamin D target neurons in the diencephalon and several brainstem nuclei suggest direct central effects of Vitamin D on sleep. It is hypothesized that sleep disorders have become an epidemic because of widespread Vitamin D deficiency.

Persistent inadequacy of Vitamin D may also increase the risk of obstructive sleep apnea via the promotion of adenotonsillar hypertrophy, muscle myopathy and/or chronic rhinitis.

In animal studies, nuclear concentrations of the Vitamin D hormone-targeted neurons have been found in specific areas of the brain and spinal cord, some of which are thought to play a role in sleep including: anterior and posterior hypothalamus, substantia nigra, midbrain central gray, raphe nuclei and the nucleus reticularis, pontis oralis and caudalis. Similar findings were reported in a study of immunohistochemical investigations with antibodies to Vitamin D receptor proteins, which found evidence for target neurons in the same regions of the brainstem and hypothalamus.

The presence of Vitamin D target neurons in these regions of the brainstem that affect sleep suggests Vitamin D may mediate an individual's sleep.

Investigations in humans into Vitamin D and sleep have also reported improved sleep outcomes with higher levels of supplemental Vitamin D.

In conclusion, we found that low levels of serum 25(OH)D in older men are associated with short sleep duration and poorer sleep efficiency. If Vitamin D does indeed play a causal role in poorer sleep, then low levels of serum 25(OH)D may put men at risk for poor sleep. Supplementation of Vitamin D in older individuals may prove to reduce the burden of poor sleep in this population.

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Vitamin D_3
(Cholecalciferol)
& Vertigo

Benign Paroxysmal Positional Vertigo (BPPV) is a relatively common condition affecting 2.4% of the general population. Frequent recurrent attacks of vertigo particularly in the elderly people affect the quality of life and result in impaired daily activities with consequent disability. Restoration of serum Vitamin D improves muscle strength in lower limbs and is expected to improve balance and fall.

Studies have shown that Espley's therapy is effective in the treatment of BPPV for a short time period but persistent improvement requires normalization of serum Vitamin D in those who have Vitamin D deficiency. Therefore, rehabilitation therapy in Vitamin D deficient patients exerts a short-term beneficial effect but the correction of deficiency with supplemental Vitamin D confers additional benefits for a longer period. Jeong et al. showed that in patients with serum Vitamin D between 10-20 ng/ml, the risk of BPPV increases 3.8 times, whereas, in patients with serum Vitamin D, less than 10 ng/ ml, the risk increases by odds of 23.

The beneficial effect of Vitamin D therapy on the severity of BPPV may be attributed to the direct effect of Vitamin D on the vestibular system or indirect effect of Vitamin D on muscle strength, fall, balance and musculoskeletal system. Serum concentrations of 25(OH)D > 30 ng/mL were consistently associated with improvement in muscle strength and balance.

This may explain the mechanistic basis of fall prevention with higher doses of Vitamin D. Optimal fall prevention has been found in studies that achieved mean serum 25(OH)D up to 75 - 100 nmol/L, whereas serum 25(OH)D < 60 nmol/L did not reduce falls. Low level of Vitamin D is associated with both low bone mass and recurrence or development of BPPV. A systematic review of seven studies demonstrated a positive correlation between low bone mass and BPPV, especially in older women.

In conclusion, researchers indicated that rehabilitation therapy of BPPV in Vitamin D deficient state exerts a beneficial effect on the severity of BPPV and the correction of Vitamin D deficiency with supplemental Vitamin D reduces recurrent attacks and provides improvement for a longer duration.

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Vitamin D_3
(Cholecalciferol)
& Geriatrics

Vitamin D can help the elderly from the vicious cycle of deficiency. Some of the reasons why our seniors are more vulnerable to Vitamin D deficiency include the decreased ability of old aged skin to produced Vitamin D, lessened Vitamin D receptors, more time spent indoors, more requirement due to weight gain, decreased/disturbed liver and kidney activity for Vitamin D processing, decreased Magnesium and decreased gut bioavailability. Moreover, seniors often take various drugs which reduce Vitamin D like statins, chemotherapy, anti-depressants, blood pressure medications, beta-blockers, etc and often have one or more diseases which consume Vitamin D (osteoporosis, diabetes, MS, etc.)

Many studies have proven that increasing Vitamin D decreases falls and fractures in the elderly by several mechanisms:

1) Improved reaction time
2) Improved muscles
3) Increased bone density

Low levels of Vitamin D were associated with substantial cognitive decline in the elderly population studied over a 6 years period, which raises important new possibilities for treatment and prevention.

Many Studies suggest that hypovitaminosis D is a risk factor for the development of depressive symptoms in older persons. The strength of the prospective association is higher in women than in men. Understanding the potential causal pathway between Vitamin D deficiency and depression requires further research.

It was therefore concluded that Vitamin D supplementation in the elderly can reduce falling and fractures, improve cognition, decrease the chance of Alzheimers and Parkinson's disease, increase the chance of surviving hospital, improve balance, reduce muscle loss, reduce flu and reduce need for antibiotics.

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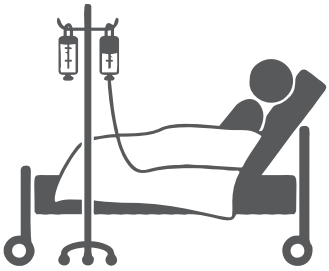
& Hospitalization



Vitamin D supplements can brighten the outlook for surgical intensive care patients and their hospital stay. A study revealed that patients who received a high daily dose of Vitamin D were less likely to experience a heart attack, had shorter hospital stays and incurred lower costs than patients receiving a lower dose.

Another study recommended that no particular side effects were reported as a result of utilizing muscular injections of Vitamin D and due to the easy and cheap use of this medicine, it can be used in the auxiliary treatment of patients with urosepsis.

Ventilator-associated pneumonia (VAP) is a common and serious problem that develops after more than 48 h of mechanical ventilation in hospitals. Improving the activity of the immune system with Vitamin D, it was indicated that Vitamin D supplementation can significantly reduce the procalcitonin in (VAP) patients, and must be considered as a preventive and/or therapeutic strategy.

Moreover, compromised immune state due to low Vitamin D status and low CD4 cell count may explain a large percentage of healthcare disparities. Aggressively optimizing serum Vitamin D status to > 40 ng/ml may be one of the most important steps in solving healthcare disparities (length of stay, costs and mortality) especially in critically injured trauma patients.

Impact of 3-monthly Vitamin D supplementation plus exercise on survival after surgery for osteoporotic hip fracture in adult patients over 50 years revealed far fewer deaths after hip fracture surgery with Vitamin D and exercise. Another demonstration was 18 fewer hospital days if given 500,000 IU of Vitamin D while ventilated in ICU. Moreover, a single dose of intramuscular cholecalciferol corrected Vitamin D deficiency in the majority of critically ill patients. Greater Vitamin D increments were associated with greater cathelicidin increases, suggesting a possible mechanism of Vitamin D supplementation in inducing bactericidal pleiotropic effects.

Therefore, the beneficial preventive and therapeutic effects of Vitamin D in hospitalized patients should not be ignored for a better prognosis, lesser hospitalization, and lower costs.

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Vitamin D_3

(Cholecalciferol)

Fact Check & Symptoms

FACT CHECK

Facts:

- Approximately 95% of our population is Vitamin D deficient[1].
- Increased prevalence of Vitamin D deficiency during winters due to lower sun positioning, darker and shorter days, increased indoor time and overprotective clothing[2].

Symptoms of Deficiency:

- Muscle Weakness
- Sleep Disturbances
- Weight Gain
- Dry Skin
- Loss of Appetite
- High Blood Pressure
- Mood Swings
- Fatigue
- Frequent Coughs & Cold
- Weak & Aching Bones
- Excessive Sweating

Majority of Pakistani population is Vitamin D3 deficient (VDD) having Vitamin D3 levels less than 20 ng/ml[3].

Vitamin D3 LEVELS
25 HYDROXY D

Deficient	Optimal*	Treat Cancer or Heart Disease	Excess
< 50ng/ml	50-70ng/ml	70-100ng/ml	> 100ng/ml

- *optimum levels for the prevention of viral infections
- < = Less than, > = Greater than

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