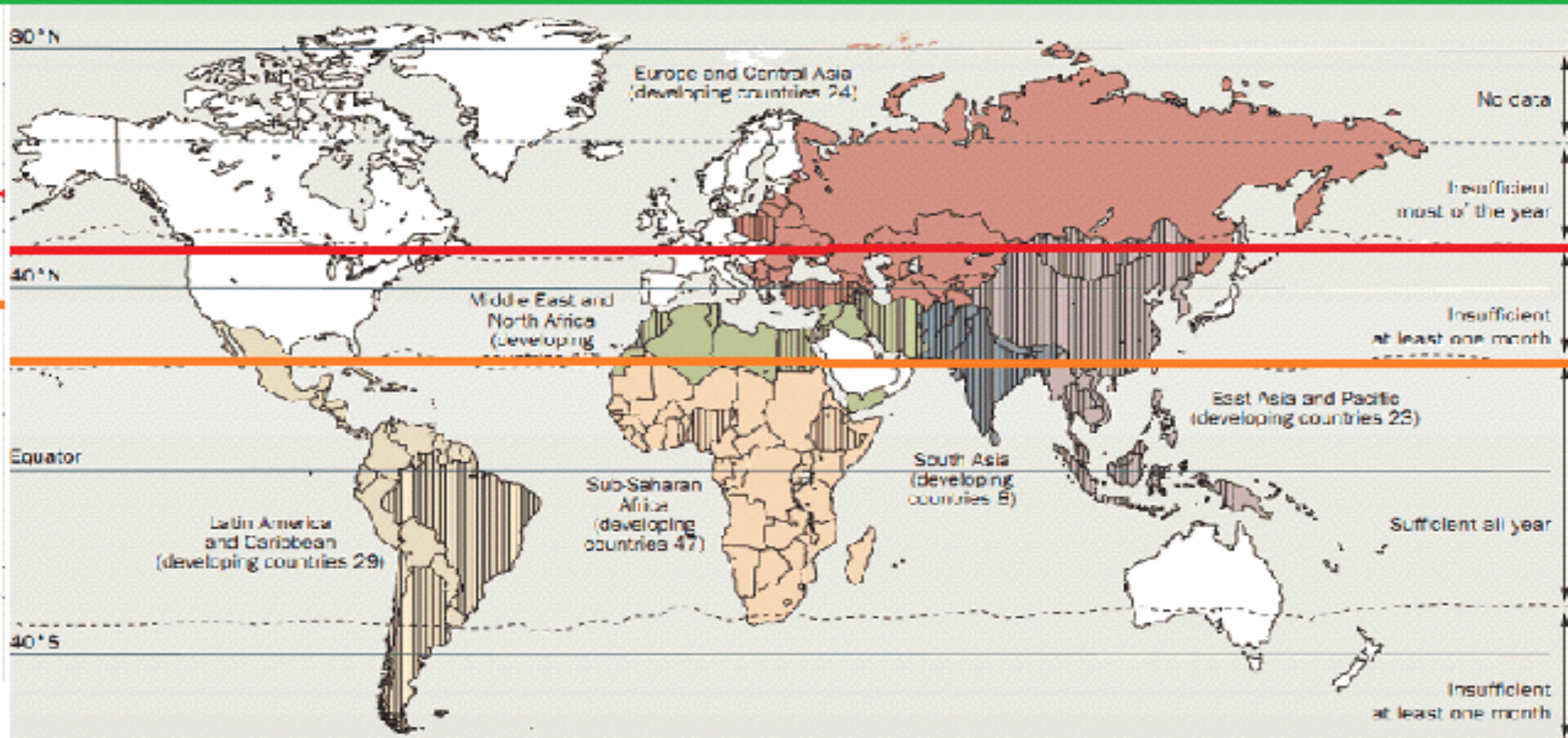
Vitamin D and VDR

Disclosure:

Relationship with commercial interests - None
Disclosure of commercial support - None
Conflict of interest - None

If you live above the orange line the sun might be too weak during winter/spring months to give you enough vitamin D, above the red line it will be very hard to be sufficient in vitamin D without food or supplements!

image taken and modified a bit from:
http://www.vitamindwiki.com/Review+of+Vitamin+D+Deficiencies+in+developing+countries+-+Oct+2011



Influence of season and latitude on the cutaneous synthesis of vitamin D3: exposure to winter sunlight in Boston and Edmonton will not promote vitamin D3 synthesis in human skin.

Webb AR[1], Kline L, Holick MF.

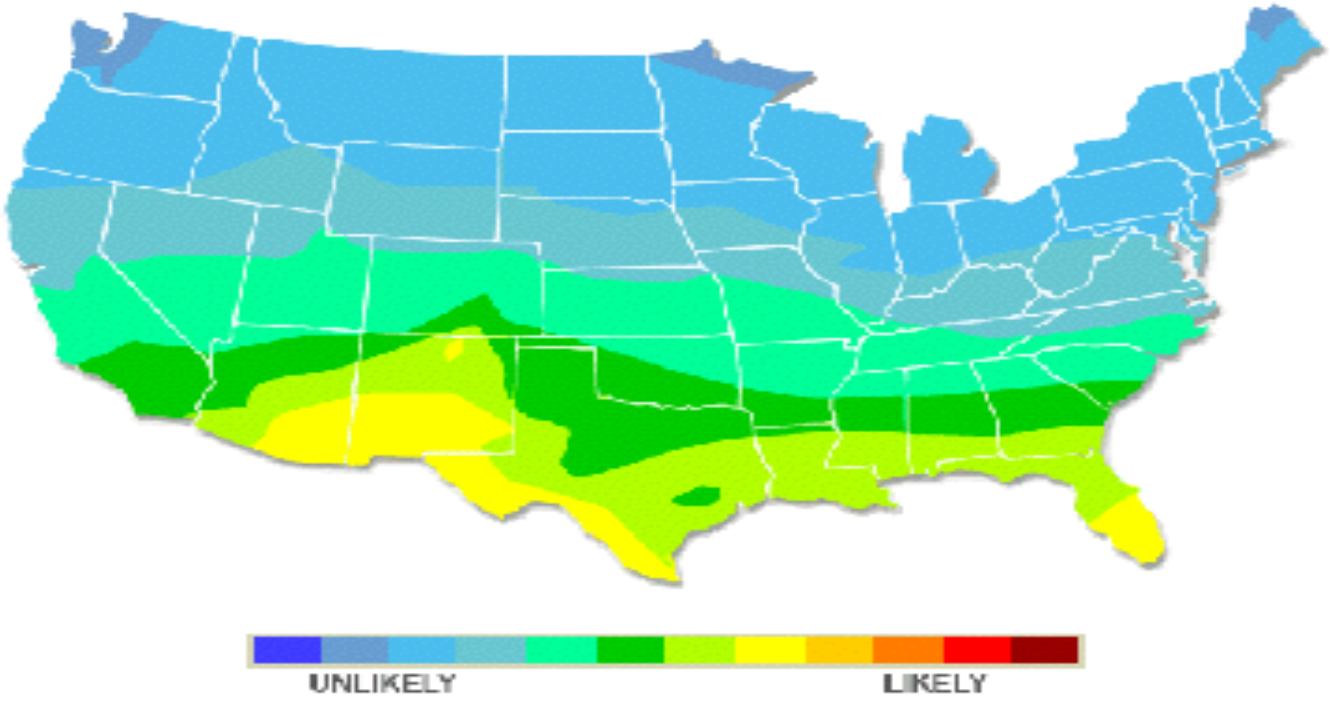
Author information

Abstract

Sunlight has long been recognized as a major provider of vitamin D for humans; radiation in the UVB (290-315 nm) portion of the solar spectrum photolyzes 7-dehydrocholesterol in the skin to previtamin D3, which, in turn, is converted by a thermal process to vitamin D3. Latitude and season affect both the quantity and quality of solar radiation reaching the earth's surface, especially in the UVB region of the spectrum, but little is known about how these influence the ability of sunlight to synthesize vitamin D3 in skin. A model has been developed to evaluate the effect of seasonal and latitudinal changes on the potential of sunlight to initiate cutaneous production of vitamin D3. Human skin or [3 alpha-3H]7-dehydrocholesterol exposed to sunlight on cloudless days in Boston (42.2 degrees N) from November through February produced no previtamin D3. In Edmonton (52 degrees N) this ineffective winter period extended from October through March. Further south (34 degrees N and 18 degrees N), sunlight effectively photoconverted 7-dehydrocholesterol to previtamin D3 in the middle of winter. These results quantify the dramatic influence of changes in solar UVB radiation on cutaneous vitamin D3 synthesis and indicate the latitudinal increase in the length of the "vitamin D winter" during which dietary supplementation of the vitamin may be advisable.

VITAMIN D SYNTHESIS

APRIL*



SOURCE: http://www.epa.gov/sunwise/uvimonth.html

*The figures provided are estimates and can vary depending on the person and/or climate changes.

Aging decreases the capacity of human skin to produce vitamin D3.

MacLaughlin J, Holick MF.

Abstract

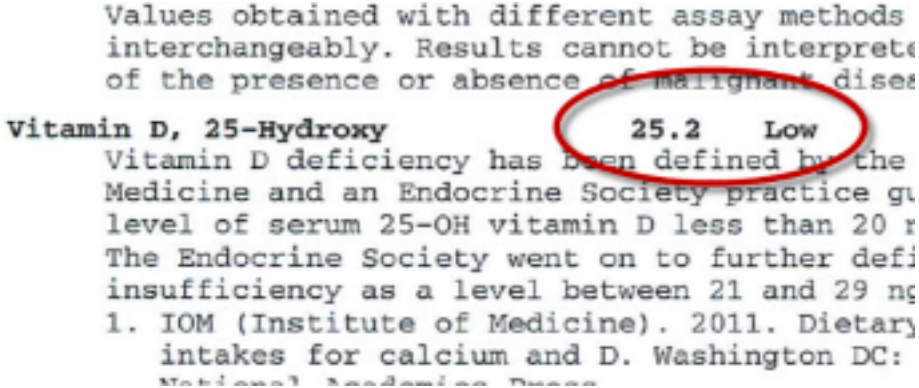
An evaluation of surgically obtained skin (age range, 8-92 yr) revealed that there is an age-dependent decrease in the epidermal concentrations of provitamin D3 (7-dehydrocholesterol). To ascertain that aging indeed decreased the capacity of human skin to produce vitamin D3, some of the skin samples were exposed to ultraviolet radiation and the content of previtamin D3 was determined in the epidermis and dermis. The epidermis in the young and older subjects was the major site for the formation of previtamin D3, accounting for greater than 80% of the total previtamin D3 that was produced in the skin. A comparison of the amount of previtamin D3 produced in the skin from the 8- and 18-yr-old subjects with the amount produced in the skin from the 77- and 82-yr-old subjects revealed that aging can decrease by greater than twofold the capacity of the skin to produce previtamin D3. Recognition of this difference may be extremely important for the elderly, who infrequently expose a small area of skin to sunlight and who depend on this exposure for their vitamin D nutritional needs.

Limitations of 25-OH Vitamin D3 Testing

- Inactive form
- SNPs
- Gene expression - influences

Solve This: 4 + ___ + 6 = ____

25-hydroxyvitamin D (25(OH)D), the precursor of the active form of vitamin D, is recognized as the optimal indicator of vitamin D metabolic status with a relatively long half-life and high concentration in plasma[5].



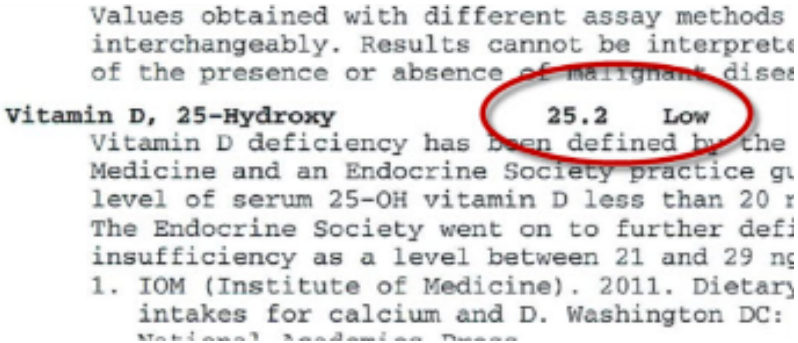
Values obtained with different assay methods
interchangeably. Results cannot be interprete
of the presence or absence of malignant dise

Vitamin D, 25-Hydroxy **25.2** **Low**

Vitamin D deficiency has been defined by the
Medicine and an Endocrine Society practice gu
level of serum 25-OH vitamin D less than 20 r
The Endocrine Society went on to further defi
insufficiency as a level between 21 and 29 ng
1. IOM (Institute of Medicine). 2011. Dietary
intakes for calcium and D. Washington DC:

http://www.nature.com/articles/srep07956

Vitamin D receptor (VDR), a key nuclear receptor, can only be activated by the free form of $1,25(OH)_2D3$, and regulates the transcription and expression of numerous vitamin D targeted genes that are related to cell proliferation, differentiation, invasion and angiogenesis.



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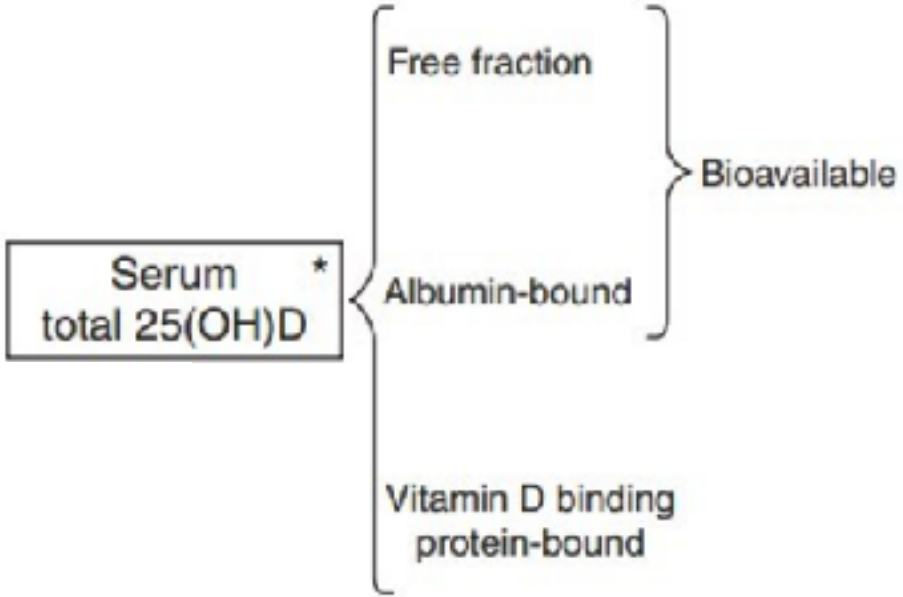
http://www.nature.com/articles/srep07956

Transport



https://www.vitamindwiki.com/Review+of+Vitamin+D+recommendations+and+knowledge+%E2%80%93+Oct+2013

Transport

The majority of 25(OH)D and $1,25(OH)_2D3$ are primarily bound to VDBP, approximately 10–15% to Alb, free 25(OH)D and $1,25(OH)_2D3$ only account for less than 1%[10]. Since the affinity of Alb to 25(OH) D or $1,25(OH)_2D3$ is weaker than that of VDBP, the loosely binding fraction and the free fraction consist of bioavailable 25(OH)D[11].

http://www.nature.com/articles/srep07956

Transport

In the absence of DBP, vitamin D metabolites are more likely to bind to albumin, which has a lower affinity for both 25OHD and $1,25(OH)_2D$ relative to DBP and will therefore be less effective in preventing urinary loss of vitamin D metabolites. Significantly, when DBP knockout mice were placed on a vitamin D deficient diet, they succumbed to bone mineralization abnormalities more rapidly than their wild type counterparts, underlining the importance of DBP in maintaining serum vitamin D concentrations under conditions of dietary restriction.

Vitamin D and DBP: The free hormone hypothesis revisited

SNPs

Vitamin D is a major regulator of gene expression and signaling in most tissues, and insufficiency affects many adults [1,2]. Genetic factors are thought to play a large part in this. Indeed, the genetic contribution to vitamin D status has been estimated to be from 28-80% [3-5]. A number of particular single nucleotide polymorphisms (SNPs) for vitamin D associated genes or particular combinations of SNPs from genes relating to vitamin D metabolism can be involved in multiple signaling pathways. These pathways can be associated with lower or higher concentrations of circulating vitamin D. These particular SNPs from genes associated with vitamin D are also becoming increasingly relevant in their association with immune disorders.

Genetic Variations in Vitamin D Metabolism Genes and the Microbiome, in the Presence of Adverse Environmental Changes, Increase Immune Dysregulation

SNPs

rs2228570	NA	G	**VDR**	Fok1	NA
rs731236	AA	G	**VDR**	Taq1	-/-
rs1544410	CC	T	**VDR**	Bsm1	-/-

SNPs

One essential component of the vitamin D pathway is the polymorphic vitamin D–binding protein (VDBP), also known as group-specific component (G_c). Aside from its main function of vitamin D transport and preservation, VDBP has been shown to scavenge actin, bind fatty acids, activate macrophages, stimulate osteoclasts, enhance the chemotactic activity of C5-derived peptides, and associate with immune cell surfaces, such as T and B cells (11). Even after ligand binding, 98–99% VDBP binding sites remain unoccupied, which suggests a function beyond vitamin D transport (11).

Reduced Serum Vitamin D–Binding Protein Levels Are Associated With Type 1 Diabetes

At the end of pregnancy, the total concentrations of 1,25-$(OH)_2D_3$ (97±26 ng/liter, n = 40) and DBP (616±84 mg/liter) are both significantly higher than in nonpregnant females and paired cord serum samples (48±11 ng/liter and 266±41 mg/liter, respectively).

Vitamin D and pregnancy: the maternal-fetal metabolism of vitamin D.

Start Digging Deep

Let's Solve This: 4 + ___ + 6 = ____

Metabolism. 2015 Mar;64(3):447-59. doi: 10.1016/j.metabol.2014.11.010. Epub 2014 Nov 29.

Concentrations of the vitamin D metabolite 1,25(OH)2D and odds of metabolic syndrome and its components.

Bea JW[1], Jurutka PW[2], Hibler EA[3], Lance P[1], Martinez ME[1], Roe DJ[5], Sardo Molmenti CL[6], Thompson PA[1], Jacobs ET[7].

Author information

Abstract

AIM: Few epidemiological studies have investigated the association between circulating concentrations of the active vitamin D metabolite 1,25(OH)2D and metabolic syndrome. We sought to determine whether blood levels of 1,25(OH)2D are associated with metabolic syndrome and its individual components, including waist circumference, triglycerides, blood pressure, and glucose, and high-density lipoprotein. We also investigated these associations for the more abundant precursor vitamin D metabolite, 25(OH)D.

METHODS: Participants from two completed clinical trials of colorectal neoplasia with available metabolic syndrome data and blood samples for measurement of 1,25(OH)2D (n=1048) and 25(OH)D (n=2096) were included. Cross-sectional analyses of the association between concentrations of 1,25(OH)2D, 25(OH)D, metabolic syndrome, and its components were conducted.

RESULTS: A statistically significant inverse association was observed for circulating concentrations of 1,25(OH)2D and metabolic syndrome, with adjusted ORs (95% CIs) of 0.73 (0.52-1.04) and 0.52 (0.36-0.75) for the second and third tertiles of 1,25(OH)2D, respectively (p-trend <0.001). Significant inverse relationships were also observed between 1,25(OH)2D and high triglycerides (p-trend <0.001), and low high-density lipoprotein (p-trend <0.001). For 25(OH)D concentrations, significant inverse associations were found for metabolic syndrome (p-trend <0.01), high waist circumference (p-trend <0.04) and triglyceride levels (p-trend <0.01). Participants with 25(OH)D ≥30 ng/ml and in the highest tertile of 1,25(OH)2D demonstrated significantly lower odds of metabolic syndrome, with an OR (95% CI) of 0.36 (0.19-0.75) compared to those in the lowest category for both metabolites.

CONCLUSION: These results provide new evidence that the relatively rarely-studied active hormonal form of vitamin D, 1,25(OH)2D, is associated with metabolic syndrome and its components, and confirm prior findings for 25(OH)D. The finding that 1,25(OH)2D is related to high-density lipoprotein, while 25(OH)D is not, suggests that there may be an independent mechanism of action for 1,25(OH)2D in relation to metabolic dysregulation.

Clin Chem Lab Med. 2017 Mar 22. pii: /j/cclm.ahead-of-print/cclm-2016-1129/cclm-2016-1129.xml. doi: 10.1515/cclm-2016-1129. [Epub ahead of print]

Impact of a single oral dose of 100,000 IU vitamin D3 on profiles of serum 25(OH)D3 and its metabolites 24,25(OH)2D3, 3-epi-25(OH)D3, and 1,25(OH)2D3 in adults with vitamin D insufficiency.

Saleh L, Tang J, Gawinecka J, Bowsch L, Fraser WD, von Eckardstein A, Nowak A.

Abstract

BACKGROUND: We investigate the effect of a high dose of vitamin D3 on circulating concentrations of 25(OH)D3 and its metabolites 24,25(OH)2D3, 3-epi-25(OH)D3, and 1,25(OH)2D3 in healthy individuals with self-perceived fatigue and vitamin D insufficiency [25(OH)D3<50 nmol/L].

METHODS: One hundred and seven study participants (age 20-50 years) were randomized to receive a single 100,000 IU dose of vitamin D3 (n=52) or placebo (n=55). Vitamin D metabolite concentrations in serum were measured before, and 4 weeks after, supplementation.

RESULTS: Overall, 52% of participants receiving vitamin D3 attained a serum 25(OH)D3 level >75 nmol/L. Among individuals who received vitamin D3, there were significant increases in serum concentrations of 25(OH)D3 and its metabolites 24,25(OH)2D3, 3-epi-25(OH)D3, and 1,25(OH)2D3 at 4 weeks; however, inter-individual variability in these changes was substantial. Positive correlations between serum 25(OH)D3 and 24,25(OH)2D3 and 3-epi-25(OH)D3, and a significant negative correlation between serum 1,25(OH)2D3 and 3-epi-25(OH)D3, were found 4 weeks after supplementation. The 24,25(OH)2D3/25(OH)D3 and 24,25(OH)2D3/1,25(OH)2D3 ratios were significantly increased, compared with baseline, in participants receiving vitamin D3. Baseline 25(OH)D3 concentration was the only factor predictive of the change in 25(OH)D3 after supplementation.

CONCLUSIONS: Administration of a single high dose of vitamin D3 leads to a significant increase in concentrations of 25(OH)D3, 24,25(OH)2D3, 3-epi-25(OH)D3 and 1,25(OH)2D3; induction of the catabolic pathway predominates over the production of 1,25(OH)2D3. Due to the high inter-individual variation in the 25(OH)D3 response to supplementation, any given dose of vitamin D is unlikely to achieve optimal vitamin D status in all treated individuals.

Severe deficiency of 1,25-dihydroxyvitamin D3 in human immunodeficiency virus infection: association with immunological hyperactivity and only minor changes in calcium homeostasis.

Haug CJ[1], Aukrust P, Haug E, Mørkrid L, Müller F, Frøland SS.

Author information

Abstract

The serum level of 1,25-dihydroxyvitamin D3 [1,25-(OH)2D], the biologically most potent metabolite of vitamin D, is tightly regulated within narrow limits in human healthy adults. 1,25-(OH)2D deficiency is rare and is associated with disturbances in calcium and bone metabolism. We have previously reported a marked decrease in serum levels of 1,25-(OH)2D in human immunodeficiency virus (HIV)-infected patients. The present study was designed to further examine the causes and consequences of severe 1,25-(OH)2D deficiency in these patients. The design was a prospective cohort study. Fifty-four HIV-infected patients clinically classified according to the revised criteria from Centers for Disease Control and Prevention and healthy controls were studied. Parameters related to vitamin D and calcium metabolism as well as immunological and nutritional status were determined. Twenty-nine of the patients (54%) had serum levels of 1,25-(OH)2D below the lower reference limit, and 18 of these had undetectable levels. In contrast, HIV-infected patients had normal serum levels of 25-hydroxyvitamin D and vitamin D-binding protein. HIV-infected patients as a group had modestly depressed serum calcium and PTH levels. There were, however, no correlations between these parameters and serum levels of 1,25-(OH)2D. There were no differences in serum calcium or PTH levels or nutritional status when patients with severe 1,25-(OH)2D deficiency were compared to other patients, but patients with undetectable 1,25-(OH)2D had significantly elevated serum phosphate levels. Furthermore, patients with undetectable 1,25-(OH)2D levels were characterized by advanced clinical HIV infection, low CD4+ lymphocyte counts, and high serum levels of tumor necrosis factor-alpha (TNFalpha). We conclude that inadequate 1alpha-hydroxylation of 25-hydroxyvitamin D seems to be the most likely cause of 1,25-(OH)2D deficiency in HIV-infected patients, possibly induced by an inhibitory effect of TNFalpha. The low 1,25-(OH)2D and high TNFalpha levels observed may impair the immune response in HIV-infected patients both independently and in combination and may represent an important feature of the pathogenesis of HIV-related immunodeficiency. Markedly depressed 1,25-(OH)2D serum levels are also present in certain other disorders characterized by immunological hyperactivity. Thus, the findings in the present study may not only represent a previously unrecognized immune-mediated mechanism for induction of 1,25-(OH)2D deficiency in human disease, but may also reflect the importance of adequate serum levels of 1,25-(OH)2D for satisfactory performance of the immune system in man.

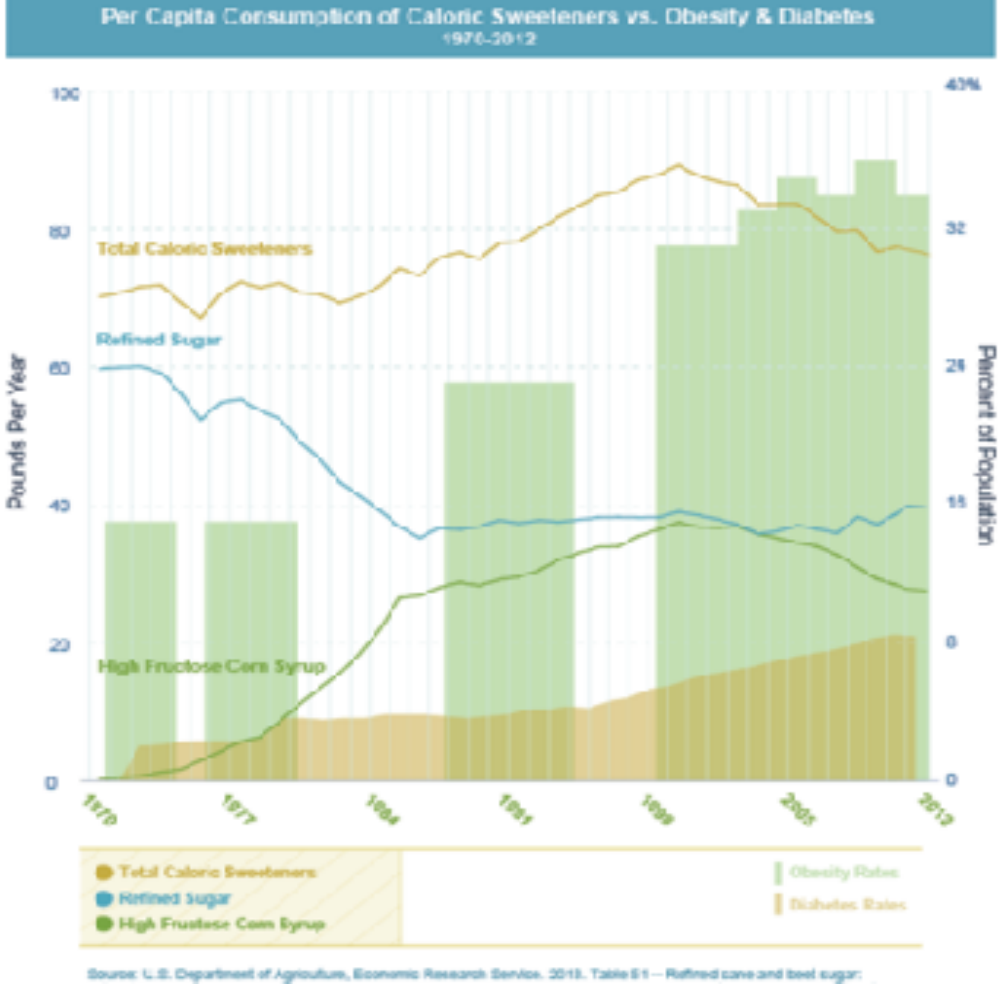
Chronic high fructose intake reduces serum 1,25 (OH)2D3 levels in calcium-sufficient rodents.

Douard V[1], Patel C[1], Lee J[1], Tanaberjasin P[1], Williams E[2], Frilton JC[3], Sabbagh Y[4], Ferraris RP[1].

Author information

Abstract

Excessive fructose consumption inhibits adaptive increases in intestinal Ca2+ transport in lactating and weanling rats with increased Ca2+ requirements by preventing the increase in serum levels of 1,25(OH)2D3. Here we tested the hypothesis that chronic fructose intake decreases 1,25(OH)2D3 levels independent of increases in Ca2+ requirements. Adult mice fed for five wk a high glucose-low Ca2+ diet displayed expected compensatory increases in intestinal and renal Ca2+ transporter expression and activity, in renal CYP27B1 (coding for 1α-hydroxylase) expression as well as in serum 1,25(OH)2D3 levels, compared with mice fed isocaloric glucose- or fructose-normal Ca2+ diets. Replacing glucose with fructose prevented these increases in Ca2+ transporter, CYP27B1, and 1,25(OH)2D3 levels induced by a low Ca2+ diet. In adult mice fed for three mo a normal Ca2+ diet, renal expression of CYP27B1 and of CYP24A1 (24-hydroxylase) decreased and increased, respectively, when the carbohydrate source was fructose instead of glucose or starch. Intestinal and renal Ca2+ transporter activity and expression did not vary with dietary carbohydrate. To determine the time course of fructose effects, a high fructose or glucose diet with normal Ca2+ levels was fed to adult rats for three mo. Serum levels of 1,25(OH)2D3 decreased and of FGF23 increased significantly over time. Renal expression of CYP27B1 and serum levels of 1,25(OH)2D3 still decreased in fructose- compared to those in glucose-fed rats after three mo. Serum parathyroid hormone, Ca2+ and phosphate levels were normal and independent of dietary sugar as well as time of feeding. Thus, chronically high fructose intakes can decrease serum levels of 1,25(OH)2D3 in adult rodents experiencing no Ca2+ stress and fed sufficient levels of dietary Ca2+. This finding is highly significant because fructose constitutes a substantial portion of the average diet of Americans already deficient in vitamin D.



(c) 2017: Dr BenLynch

Cell Mol Life Sci. 2010 Dec;67(24):4249-56. doi: 10.1007/s00018-010-0441-4. Epub 2010 Jul 1.

Epstein-Barr virus encoded EBNA-3 binds to vitamin D receptor and blocks activation of its target genes.

Yenamandra SP[1], Hellman U, Kempkes B, Darekar SD, Petermann S, Sculley T, Klein G, Kashuba E.

Author information

Abstract

Epstein-Barr virus (EBV) is a human gamma herpes virus that infects B cells and induces their transformation into immortalized lymphoblasts that can grow as cell lines (LCLs) in vitro. EBNA-3 is a member of the EBNA-3-protein family that can regulate transcription of cellular and viral genes. The identification of EBNA-3 cellular partners and a study of its influence on cellular pathways are important for understanding the transforming action of the virus. In this work, we have identified the vitamin D receptor (VDR) protein as a binding partner of EBNA-3. We found that EBNA3 blocks the activation of VDR-dependent genes and protects LCLs against vitamin-D3-induced growth arrest and/or apoptosis. The presented data shed some light on the anti-apoptotic EBV program and the role of the EBNA-3-VDR interaction in the viral strategy.

Another factor linked to *VDR* and which may also contribute to the inflammatory process in conditions like CD, is the ability of some pathogenic bacteria to bind to and inactivate the *VDR* receptor. By doing this, they disarm the innate immune response and thus also increase the risk of inflammation. Gliding biofilm bacteria have been shown to produce a sulfonolipid capnine (2-amino-3-hydroxy-15-methylhexadecane-1-sulfonic acid) which acts as a nanomolar kinetic inhibitor on the *VDR* ligand binding pocket [64,65]. Other examples of bacteria that are able to reduce the expression of *VDR* are Borrelia burgdorferi, Chlamydia trachomatis, Mycobacterium leprae

Polyunsaturated fatty acids decrease the apparent affinity of vitamin D metabolites for human vitamin D-binding protein.

Bouillon R[1], Xiang DZ, Convents R, Van Baelen H.

⊕ Author information

Abstract

The affinity of purified human vitamin D-binding protein from serum (DBP) for 25-hydroxyvitamin D3 (25-OHD3) and 1 alpha,25-dihydroxyvitamin D3 [1,25-(OH)2D3] was measured in the presence of free fatty acids (FFA), cholesterol, prostaglandins and several drugs. Mono- and polyunsaturated fatty acids markedly decreased the affinity of both 25-OHD3 and 1,25-(OH)2D3 for DBP, whereas saturated fatty acids (stearic and arachidic acid), cholesterol, cholesterol esters, retinol, retinoic acid and prostaglandins (A1 and E1) did not affect the apparent affinity. Several chemicals known to decrease the binding of thyroxine to its plasma-binding protein did not affect the affinity of DBP. The apparent affinity of DBP for both 25-OHD3 and 1,25-(OH)2D3 decreased 2.4- to 4.6-fold in the presence of 36 microM of linoleic or arachidonic acid, respectively. Only a molar ratio of FFA:DBP higher than 10,000 was able to decrease the binding of 25-OHD3 to DBP by 20%. Much smaller ratio's of FFA:DBP (25 for arachidonic and 45 for oleic acid), however, decreased the binding of 1,25-(OH)2D3 to DBP. These latter ratio's are well within the physiological range. The addition of human albumin in a physiological albumin:DBP molar ratio did not impair the inhibitory effect of linoleic acid on the binding of [3H]25-OHD3 to DBP. The binding and bioavailability of vitamin D metabolites thus might be altered by mono- and polyunsaturated but not by saturated fatty acids.

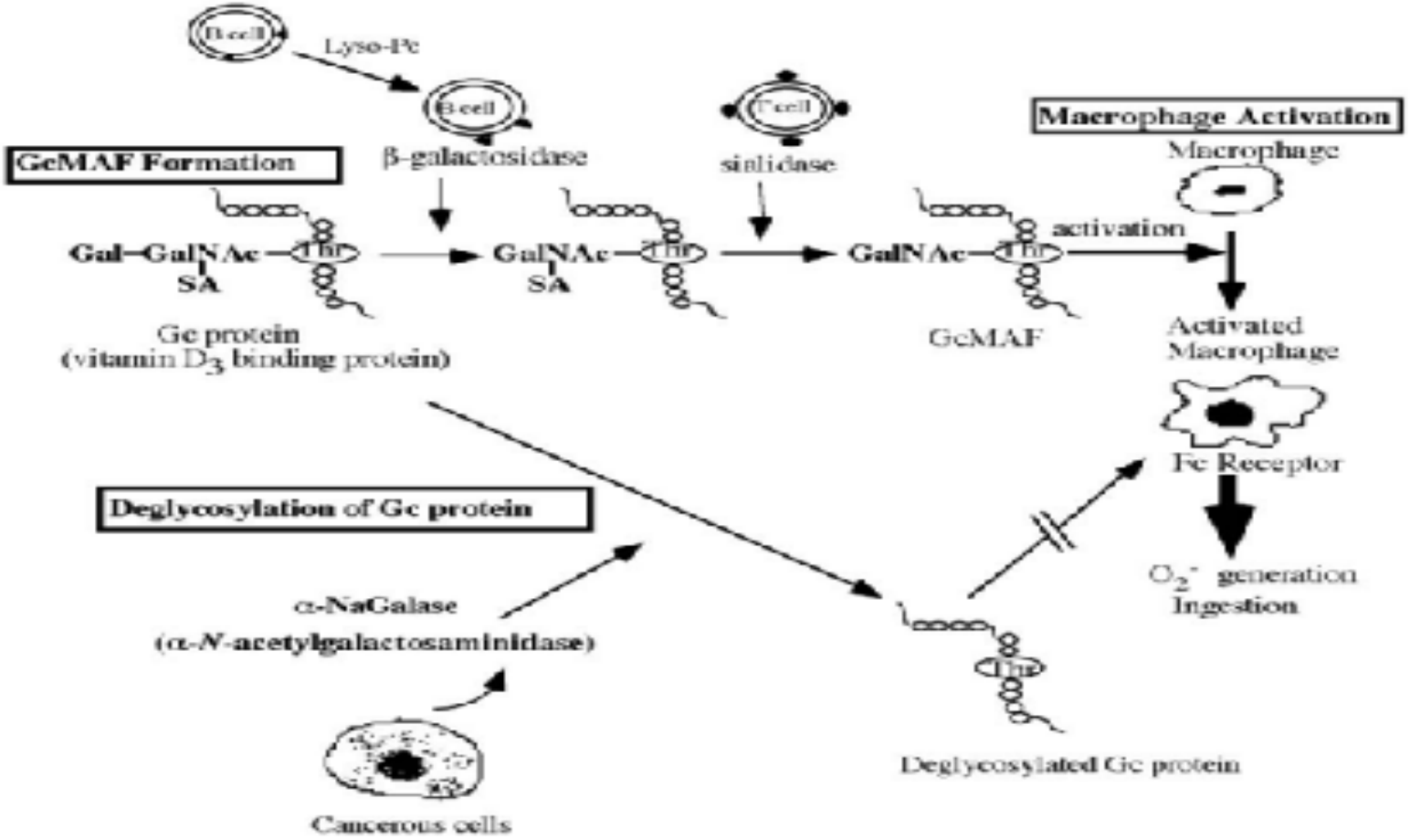


Figure 2. *Cascade from Gc protein to GcMAF and deglycosylation of Gc protein.*

Immunotherapy of metastatic colorectal cancer with vitamin D-binding protein-derived macrophage-activating factor, GcMAF.

Yamamoto N[1], Suyama H, Nakazato H, Yamamoto N, Koga Y.

⊕ Author Information

Retraction in

Retraction note to: Immunotherapy of metastatic colorectal cancer with vitamin D-binding protein-derived macrophage-activating factor, GcMAF. [Cancer Immunol Immunother. 2014]

Abstract

Serum vitamin D binding protein (Gc protein) is the precursor for the principal macrophage-activating factor (MAF). The MAF precursor activity of serum Gc protein of colorectal cancer patients was lost or reduced because Gc protein is deglycosylated by serum alpha-N-acetylgalactosaminidase (Nagalase) secreted from cancerous cells. Deglycosylated Gc protein cannot be converted to MAF, leading to immunosuppression. Stepwise treatment of purified Gc protein with immobilized beta-galactosidase and sialidase generated the most potent macrophage-activating factor (GcMAF) ever discovered, but it produces no side effect in humans. Macrophages treated with GcMAF (100 microg/ml) develop an enormous variation of receptors and are highly tumoricidal to a variety of cancers indiscriminately. Administration of 100 nanogram (ng)/ human maximally activates systemic macrophages that can kill cancerous cells. Since the half-life of the activated macrophages is approximately 6 days, 100 ng GcMAF was administered weekly to eight nonanemic colorectal cancer patients who had previously received tumor-resection but still carried significant amounts of metastatic tumor cells. As GcMAF therapy progressed, the MAF precursor activities of all patients increased and conversely their serum Nagalase activities decreased. Since serum Nagalase is proportional to tumor burden, serum Nagalase activity was used as a prognostic index for time course analysis of GcMAF therapy. After 32-50 weekly administrations of 100 ng GcMAF, all colorectal cancer patients exhibited healthy control levels of the serum Nagalase activity, indicating eradication of metastatic tumor cells. During 7 years after the completion of GcMAF therapy, their serum Nagalase activity did not increase, indicating no recurrence of cancer, which was also supported by the annual CT scans of these patients.

Lab Testing

Serum 1,25 OH D2 Sample Handling

25-Hydroxyvitamin D will also be measured on the same sample, since results for 1,25-dihydroxyvitamin D cannot be interpreted without this information. The assays measure both the D3 and D2 forms of the vitamin

Patient Preparation

None. No special dietary restriction is necessary. Take blood (5 mL) into a syringe or red-topped vacutainer.

Sample Preparation

Transfer the blood to a plain glass tube and allow to clot for 30 min. If using a vacutainer, allow blood to clot in vacutainer. Freeze the serum (-20C) promptly. Send serum (2 mL) to the SAS laboratory. Ensure the sample remains frozen during transport.

http://www.sas-centre.org/assays/hormones/25-hydroxyvitamin-d-with-125-dihydroxyvitamin-d

Turnaround time: 1 day (Set up every Tuesday)

Reference Range (Adults):

Bioavailable Vitamin D	: 1.92 – 8.82	ng / ml
Vitamin D Binding protein	: 104 – 477	ug / ml
Calculated free Vitamin D	: 5 – 18	pg / ml
Total Vitamin D (25 Hydroxy)	: 15 – 60	ng / ml

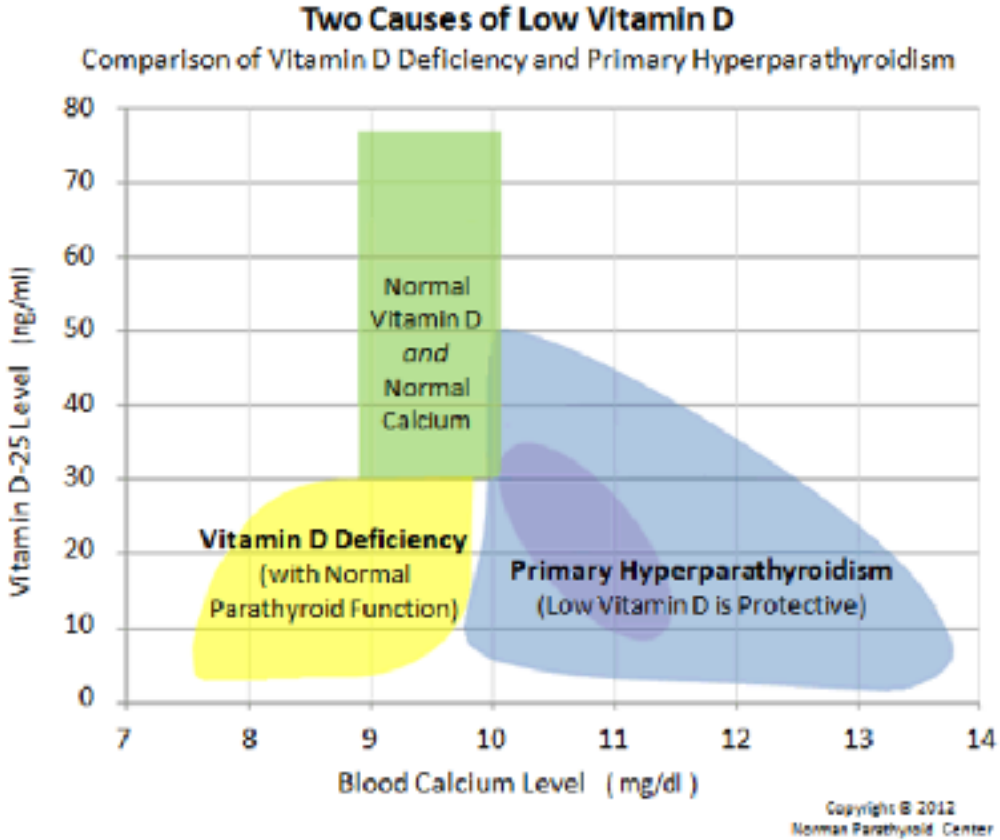
Turnaround time: 2 days (Set up every Tuesday)

Reference Range (Adults): Bioavailable Vitamin D (1, 25 dihydroxy)
: 3.4 – 14.2 pg / ml

Vitamin D Binding protein	: 104 – 477	ug / ml
Calculated free Vitamin D (1, 25 dihydroxy)	: 0.1 – 0.44	pg /ml
Total Vitamin D (1, 25 dihydroxy)	: 15 – 80	pg / ml

http://panlaboratories.com/bioavailable-vitamin-d-1-25-dihydroxy/

Serum High Phosphate



http://www.parathyroid.com/low-vitamin-d.htm

Vitamin D in Patients with PRIMARY Hyperparathyroidism

We began measuring Vitamin D levels in patients with hyperparathyroidism in the mid-1990's. For the past several years, we have measured it in most patients, and beginning in 2003 we began measuring Vitamin D in every patient with PRIMARY hyperparathyroidism. Here is what we found in our recently published article on 10,000 patients with primary hyperparathyroidism:

★ **84% of all patients with primary hyperparathyroidism will have LOW Vitamin D-25 Levels!** This is 8,397 patients out of 10,000 in our study. 3812 patients (38%) had levels **below 20** ng/ml with an average Vitamin D level of 14.6. A more recent study by our group in 25,000 patients showed 92% of patients with a parathyroid tumor and primary hyperparathyroidism have low Vitamin D-25.

★ **The average Vitamin D level in patients with a parathyroid tumor removed at surgery was 21.4**

★ **Less than 10% of all patients with primary hyperparathyroidism will have NORMAL Vitamin D-25 Levels (above 30).** Their average Vitamin D level was 35.3 ng/ml. (Note that some patients will have normal vitamin D levels because they have been taking vitamin D when the test was done).

★ **0 % of all patients with primary hyperparathyroidism will have HIGH Vitamin D-25 Levels** We've never seen it in over 30,000 patients with parathyroid tumors.

★ **As the calcium level increases, the level of Vitamin D-25 decreases.** The following graph shows this nicely. When we look at 18,000 patients with a parathyroid tumor (we know it because we removed the tumor and gave the patient a picture of it), we see that those with higher calcium levels tend to have lower Vitamin D-25 levels. As you will read below, this is because the body is trying to protect itself from the high calcium, and it is converting one form of Vitamin D (Vit-D-25) into another form (Vit-D-1-25). The body is protecting itself from the high calcium by trying to get rid of the vitamin D. It does this by decreasing the amount of overall Vitamin D in our body so we don't absorb as much calcium in our diet. As you can see from the graph below, the higher a patient's calcium goes, the lower the Vitamin D-25 goes.

http://www.parathyroid.com/low-vitamin-d.htm

Serum High Phosphate

History

Typically, most patients with hyperphosphatemia are asymptomatic. Signs and symptoms of acute hyperphosphatemia result from the effects of hypocalcemia, with patients occasionally reporting symptoms such as muscle cramps, tetany, and perioral numbness or tingling. Other symptoms include bone and joint pain, pruritus, and rash.

More commonly, patients report symptoms related to the underlying cause of the hyperphosphatemia, generally uremic symptoms such as fatigue, shortness of breath, anorexia, nausea, vomiting, and sleep disturbances.

Therefore, information related to the causes of hyperphosphatemia, such as a history of diabetes mellitus or hypertension (causes of renal failure), a history of neck surgery or irradiation (causes of hypoparathyroidism), or a history of excessive vitamin D or milk ingestion, is important to obtain.

http://emedicine.medscape.com/article/241185-clinical

High Phosphate

The patient's medication history with regard to the following should also be obtained:

- Oral phosphate binders
- Potassium phosphate
- Antacids
- Bisphosphonates
- Laxatives (oral/rectal) and enemas [38]
- Nutritional supplements or hyperalimentation

http://emedicine.medscape.com/article/241185-clinical

High Phosphate

A raised serum phosphate can be caused by:

a. excessive intake (for example phosphate-containing laxatives and enemas),
b. excessive absorption (caused by high vitamin D intake),
c. redistribution after tissue destruction (for example after chemotherapy),
d. acidosis (phosphate ions move out of cells into the extra-cellular fluid),
e. low insulin activity – diabetes mellitus,
f. poor excretion (renal failure)
g. hypoparathyroidism (in which there is increased tubular reabsorption of phosphate).

Females subject values are generally slightly higher than those of males. Serum phosphate levels are higher in children and neonates than they are in adults, but otherwise values are constant throughout life.

Interpretation

Phosphate is absorbed from the small intestine under the control of PTH and vitamin D. The excretion of phosphate is controlled in the kidney. Phosphate is reabsorbed in the proximal tubule via a sodium-dependent transporter, with fine control by PTH (which inhibits phosphate reabsorption) in the distal tubule. There is a circadian rhythm in serum phosphate. Results are highest in the late morning and higher in summer than in winter.

http://www.biolab.co.uk/docs/phosphat.pdf

Bottom Line

Measure 25 OH Vitamin D3 + 1,25 OH Vitamin D3

Evaluate renal and liver function

Evaluate serum PTH if suspect

Lifestyle factors: fructose, sun, pregnancy, stress, diet, malabsorption

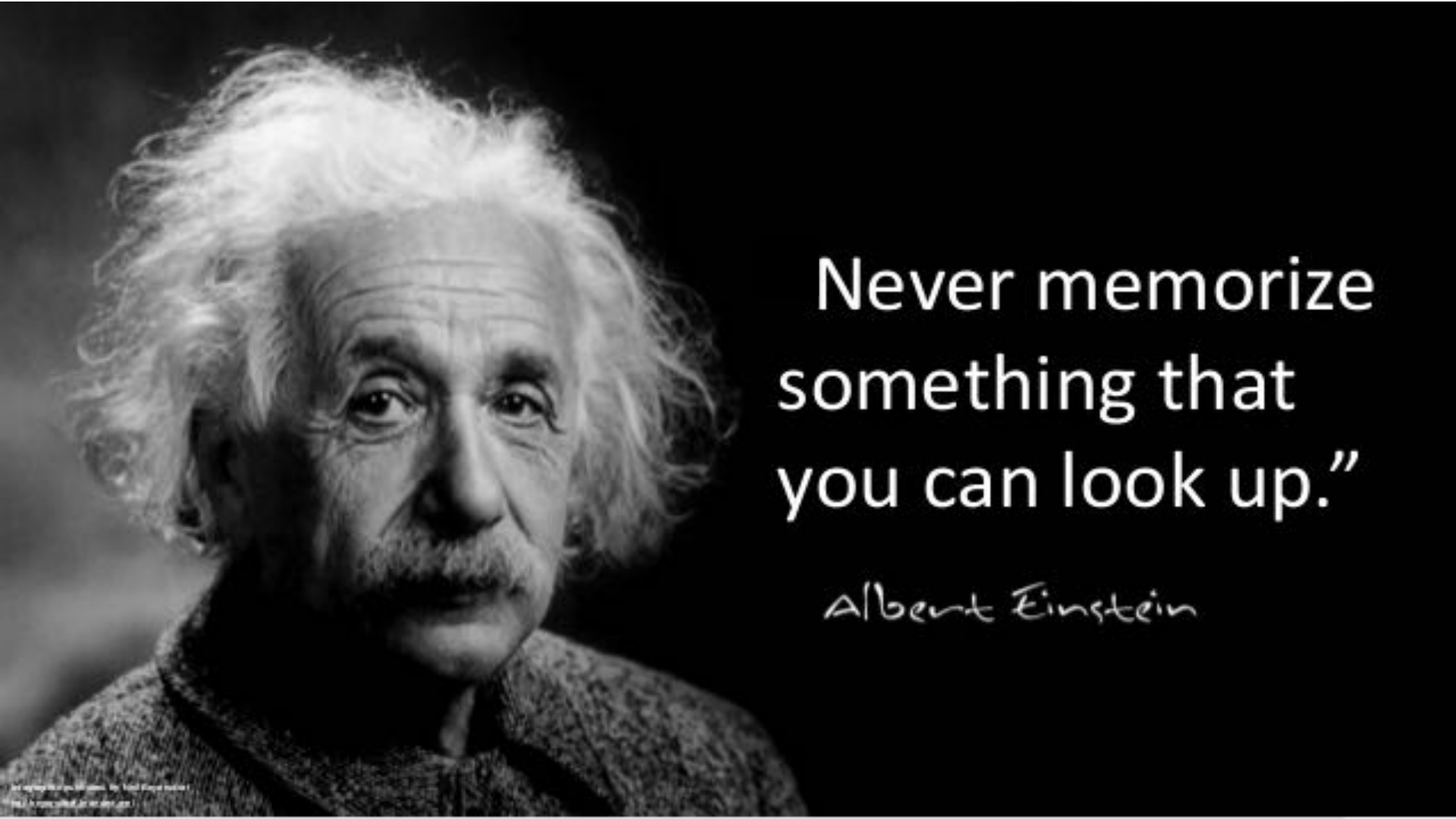
Evaluate hsCRP, lipid peroxides, serum phosphate, LPS

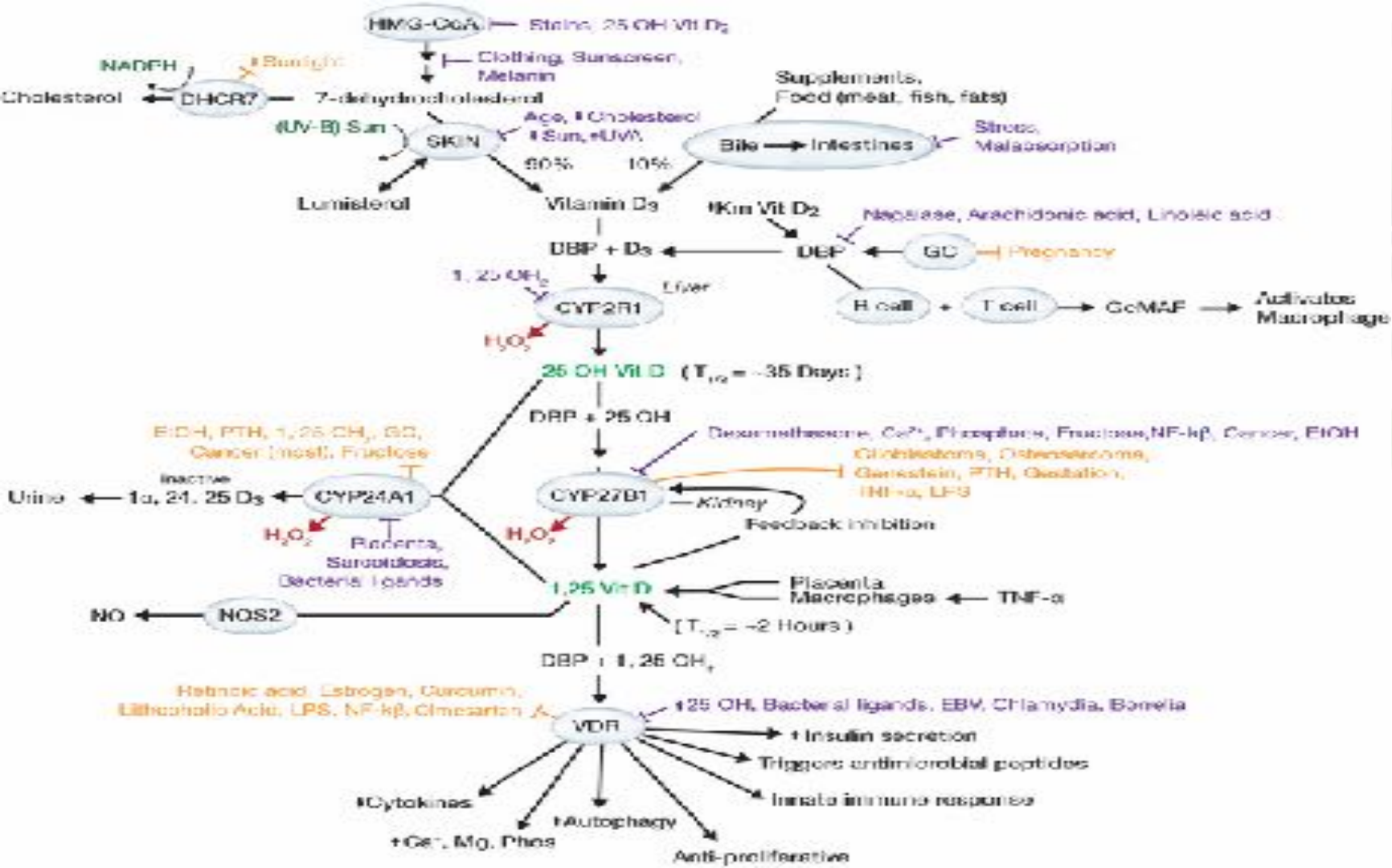
Identify infection areas – gut, blood, nose, mouth, skin, ear, STD

Identify all infection types – mold, yeast, viral, bacterial, parasite, lyme

Evaluate Vitamin D SNPs?

Solve This: 4 + 10 + 6 = ____


Never memorize
something that
you can look up.”
Albert Einstein


HMG-CoA
Statins, 25 OH Vit D3
NADPH
Sunlight
Clothing, Sunscreen, Melanin
Cholesterol
DHCR7
7-dehydrocholesterol
Supplements, Food (meat, fish, fats)
(UV-B) Sun
SKIN
Age, ↓ Cholesterol ↓ Sun, ↑UVA
Bile → Intestines
Stress, Malabsorption
90%
10%
Lumisterol
Vitamin D3
↑Kin Vit D2
Necrase, Arachidonic acid, Linoleic acid
DBP + D3
DBP
GC
Pregnancy
1, 25 OH2
Liver
CYP2R1
B cell + T cell → GcMAF → Activates Macrophage
H2O2
25 OH Vit D (T1/2 = ~35 Days:)
DBP + 25 OH
Dexamethasone, Ca2+, Phosphates, Fructose, NF-kβ, Cancer, EtOH
Glioblastoma, Osteosarcoma, Genistein, PTH, Oestrogen, TNF-α, LPS
Inactive
Urine
1α, 24, 25 D3
CYP24A1
CYP27B1
Kidney
Feedback Inhibition
H2O2
H2O2
Bacteria, Sarcoidosis, Bacterial Ligands
1,25 Vit D
Placenta Macrophages
TNF-α
NO
NOS2
(T1/2 = ~2 Hours)
DBP + 1, 25 OH2
Retinoic acid, Estrogen, Curcumin, Lithocholic Acid, LPS, NF-kβ, Olmesartan
VDR
↑25 OH, Bacterial ligands, EBV, Chlamydia, Borrelia
↑ Insulin secretion
Triggers antimicrobial peptides
Innate immune response
↓Cytokines
↑Autophagy
↑Ca2+, Mg, Phos
Anti-proliferative

References

All papers shown in presentation are published in PubMed and cited. References are either at footer presented as a link or is the title of the abstract shown.

Other citations are provided as links on footer of each slide. All diagrams shown have references organized by pathway and gene.

References may be found here:
https://seekinghealth.org/bibliography/