Vitamin D
Literature review

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Contents

Vitamin D - Important literature references

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1. CLINICAL

The quantity of papers on the clinical outcomes of Vitamin D deficiency or supplementation is enormous. Hereafter are presented some of the most pertinent recent papers.
Many references can also be found on http://www.vitamindcouncil.org/.

- HOLICK M.F. (2006)

Resurrection of Vitamin D deficiency and rickets.
J. Clin. Invest., 116:2062-2072.

Vitamin D–deficiency rickets is a sunlight deficiency disease. The inability to appreciate the beneficial effect of sunlight for health had devastating consequences for both children and adults for more than 300 years. When it was finally realized that exposure to sunlight could prevent and treat rickets, this led to the recommendation that all children be exposed to sensible sunlight to maximize bone health. The fortification of milk with vitamin D eradicated rickets as a major health problem, and, therefore, it was thought to have been conquered.

- HOLICK M.F. (2006)

High prevalence of vitamin D inadequacy and implications for health.
Mayo Clin. Proc., 81(3):353–73.

During the past decade, major advances have been made in vitamin D research that transcend the simple concept that vitamin D is Important for the prevention of rickets in children and has little physiologic relevance for adults. Inadequate vitamin D, in addition to causing rickets, prevents children from attaining their genetically programmed peak bone mass, contributes to and exacerbates osteoporosis in adults, and causes the often painful bone disease osteomalacia. Adequate vitamin D is also important for proper muscle functioning, and controversial evidence suggests it may help prevent type 1 diabetes mellitus, hypertension, and many common cancers. Vitamin D inadequacy has been reported in approximately 36% of otherwise healthy young adults and up to 57% of general medicine inpatients in the United States and in even higher percentages in Europe. Recent epidemiological data document the high prevalence of vitamin D inadequacy among elderly patients and especially among patients with osteoporosis. Factors such as low sunlight exposure, age-related decreases in cutaneous synthesis, and diets low in vitamin D contribute to the high prevalence of vitamin D inadequacy. Vitamin D production from cutaneous synthesis or intake from the few vitamin D-rich or enriched foods typically occurs only intermittently. Supplemental doses of vitamin D and sensible sun exposure could prevent deficiency in most of the general population. The purposes of this article are to examine the prevalence of vitamin D inadequacy and to review the potential implications for skeletal and extraskeletal health.

- HOLICK M.F. (2007)

Vitamin D Deficiency.
N. Engl. J. Med., 357:266-281.

- CHUNG M. (2009)

Vitamin D and calcium: a systematic review of health outcomes. Evidence report/technology assessment.
Evid. Rep. Technol. Assess., 183:1-420.

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We summarized 165 primary articles and 11 systematic reviews that incorporated over 200 additional primary articles. Available evidence focused mainly on bone health, cardiovascular diseases or cancer outcomes. For many outcomes, it was difficult to draw firm conclusions on the basis of the available literature concerning the association of either serum 25(OH)D concentration or calcium intake, or the combination of both nutrients. Findings were inconsistent across studies for colorectal and prostate cancer, and pregnancy-related outcomes including preeclampsia. There were few studies for pancreatic cancer and immune function. Among trials of hypertensive adults, calcium supplementation lowered systolic, but not diastolic, blood pressure by 2-4 mm Hg. For body weight, the trials were consistent in finding no significant effect of increased calcium intake on weight. For growth rates, a meta-analysis did not find a significant effect on weight or height gain attributable to calcium supplement in children. For bone health, one systematic review found that vitamin D plus calcium supplementation resulted in small increases in BMD of the spine and other areas in postmenopausal women. For breast cancer, calcium intakes in premenopausal women were associated with a decreased risk. For prostate cancer, some studies reported that high calcium intakes were associated with an increased risk.
The majority of the findings concerning vitamin D, calcium, or a combination of both nutrients on the different health outcomes were inconsistent. Synthesizing a dose-response relation between intake of either vitamin D, calcium, or both nutrients and health outcomes in this heterogeneous body of literature proved challenging.

- KULIE T. (2009)

Vitamin D: an evidence-based review.
J. Am. Board Fam. Med., 22(6):698-706.

Vitamin D is a fat-soluble vitamin that plays an important role in bone metabolism and seems to have some anti-inflammatory and immune-modulating properties. In addition, recent epidemiologic studies have observed relationships between low vitamin D levels and multiple disease states. Low vitamin D levels are associated with increased overall and cardiovascular mortality, cancer incidence and mortality, and autoimmune diseases such as multiple sclerosis. Although it is well known that the combination of vitamin D and calcium is necessary to maintain bone density as people age, vitamin D may also be an independent risk factor for falls among the elderly. New recommendations from the American Academy of Pediatrics [corrected] address the need for supplementation in breastfed newborns and many questions are raised regarding the role of maternal supplementation during lactation. Unfortunately, little evidence guides clinicians on when to screen for vitamin D deficiency or effective treatment options.

- PITTAS A.G. (2010)

Vitamin D and Cardiometabolic Outcomes: A Systematic Review.
Ann. Intern. Med., 152(5):307–14.

In conclusion, a lower vitamin D status was possibly associated with higher risk of incident hypertension and cardiovascular disease, but the association with diabetes-related outcomes remains unclear. As a whole, trials showed no statistically significant effect of vitamin D supplementation on cardiometabolic outcomes. The available data are inadequate to support the contention that cardiometabolic outcomes can be improved by raising vitamin D intake or serum or plasma 25(OH)D concentrations. It is therefore imperative that adequate randomized trials are conducted in well-defined populations (e.g. pre-diabetes, pre-hypertension, whites vs. non-whites) to test the potential role of vitamin D in primary prevention or therapy. Vitamin D remains a promising, though unproven, new element in the prevention and management of cardiometabolic disease.

- AUTIER P. (2013)

Vitamin D status and ill health: a systematic review.

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Lancet Diabetes Endocrinol., 2(1):76-89.

Low serum concentrations of 25-hydroxyvitamin D (25[OH]D) have been associated with many non-skeletal disorders. However, whether low 25(OH)D is the cause or result of ill health is not known. We did a systematic search of prospective and intervention studies that assessed the effect of 25(OH)D concentrations on non-skeletal health outcomes in individuals aged 18 years or older. We identified 290 prospective cohort studies (279 on disease occurrence or mortality, and 11 on cancer characteristics or survival), and 172 randomised trials of major health outcomes and of physiological parameters related to disease risk or inflammatory status. Investigators of most prospective studies reported moderate to strong inverse associations between 25(OH)D concentrations and cardiovascular diseases, serum lipid concentrations, inflammation, glucose metabolism disorders, weight gain, infectious diseases, multiple sclerosis, mood disorders, declining cognitive function, impaired physical functioning, and all-cause mortality. High 25(OH)D concentrations were not associated with a lower risk of cancer, except colorectal cancer. Results from intervention studies did not show an effect of vitamin D supplementation on disease occurrence, including colorectal cancer. In 34 intervention studies including 2805 individuals with mean 25(OH)D concentration lower than 50 nmol/L at baseline supplementation with 50 µg per day or more did not show better results. Supplementation in elderly people (mainly women) with 20 µg vitamin D per day seemed to slightly reduce all-cause mortality. The discrepancy between observational and intervention studies suggests that low 25(OH)D is a marker of ill health. Inflammatory processes involved in disease occurrence and clinical course would reduce 25(OH)D, which would explain why low vitamin D status is reported in a wide range of disorders. In elderly people, restoration of vitamin D deficits due to ageing and lifestyle changes induced by ill health could explain why low-dose supplementation leads to slight gains in survival.

- ANGLIN R.E. (2013)

Vitamin D deficiency and depression in adults: systematic review and meta-analysis.
Br. J. Psychiatry, 202:100-107.

One case-control study, ten cross-sectional studies and three cohort studies with a total of 31 424 participants were analysed. Lower vitamin D levels were found in people with depression compared with controls (SMD = 0.60, 95% CI 0.23-0.97) and there was an increased odds ratio of depression for the lowest v. highest vitamin D categories in the cross-sectional studies (OR = 1.31, 95% CI 1.0-1.71). The cohort studies showed a significantly increased hazard ratio of depression for the lowest v. highest vitamin D categories (HR = 2.21, 95% CI 1.40-3.49).
Our analyses are consistent with the hypothesis that low vitamin D concentration is associated with depression, and highlight the need for randomised controlled trials of vitamin D for the prevention and treatment of depression to determine whether this association is causal.

- BOLLAND M.J. (2014)

The effect of vitamin D supplementation on skeletal, vascular, or cancer outcomes: a trial sequential meta-analysis.
Lancet Diabetes Endocrinol., 2(4):307-320.

Our findings suggest that vitamin D supplementation with or without calcium does not reduce skeletal or non-skeletal outcomes in unselected community-dwelling individuals by more than 15%. Future trials with similar designs are unlikely to alter these conclusions.

- THEODORATOU E. (2014)

Vitamin D and multiple health outcomes: umbrella review of systematic reviews and meta-analyses of observational studies and randomised trials.

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BMJ, 348(7952):12.

In conclusion, although vitamin D has been extensively studied in relation to a range of outcomes and some indications exist that low plasma vitamin D concentrations might be linked to several diseases, firm universal conclusions about its benefits cannot be drawn. Observational studies have identified links with several diseases, but these have either not been evaluated or not been replicated in randomised controlled trials. Randomised controlled trials for autoimmune and cancer related outcomes are clearly lacking. In addition, earlier evidence from randomised controlled trials that vitamin D supplementation (with or without calcium) increases bone mineral density and reduces the risk of fractures in older people is not seen in clinical trials that examine vitamin D only supplementation. On the basis of the results of this review, an association between vitamin D concentrations and birth weight, dental caries in children, maternal vitamin D concentrations at term, and parathyroid hormone concentrations in patients with chronic kidney disease requiring dialysis is probable, but further studies and better designed trials are needed to draw firmer conclusions.

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2. MEASUREMENT OF VITAMIN D

- WALLACE A.M. (2010)

Measurement of 25-hydroxyvitamin D in the clinical laboratory: Current procedures, performance characteristics and limitations.
Steroids, 75(7):477-88.

In this review we describe procedures, performance characteristics and limitations of methods available for the measurement of 25-hydroxyvitamin (25OHD) since the year 2000. The two main types of methods are competitive immunoassay and those based on chromatographic separation followed by non-immunological direct detection (HPLC, LC–MS/MS). Lack of a reference standard for 25OHD has, until recently, been a major issue resulting in poor between-method comparability. Fortunately this should soon improve due to the recent introduction of a standard reference material in human serum (SRM 972) from the National Institute of Standards and Technology (NIST). For immunoassay, specificity can be an issue especially in relation to the proportion of 25OHD2 that is quantified whereas HPLC and LC–MS/MS methods are able to measure the two major vitamin D metabolites 25OHD2 and 25OHD3 independently. HPLC and LC–MS/MS require more expensive equipment and expert staff but this can be offset against lower reagent costs. Looking to the future it is hoped that the imminent introduction of a standard reference method (or methods) for 25OHD will further accelerate improvements in between method comparability.

- CAVALIER E. (2011)

Cross-reactivity of 25-hydroxy vitamin D2 from different commercial immunoassays for 25-hydroxy vitamin D: an evaluation without spiked samples.
Clin. Chem. Lab. Med., 49(3):555-558.

Thus, we evaluated the cross-reactivity for 25OHD2 in six commercially available kits without samples spiked with 25OHD2. We confirmed that the Roche Elecsys assay cross-reacted extremely poorly with 25OHD2, as described by the manufacturer. Compared to LC-MS/MS, all the other tested kits showed approximately 100% cross-reactivity with 25OHD2.

- CARTER G. (2011)

Accuracy of 25-Hydroxyvitamin D Assays: Confronting the Issues.
Current Drug Targets, 12(1):19-28.

The Vitamin D External Quality Assessment Scheme (DEQAS) has revealed method-related differences in 25-OHD results, raising concerns about the comparability and accuracy of different assays. This paper highlights some of the pre-analytical, analytical and post-analytical issues which may influence the accuracy of 25-OHD assays and interpretation of results. Data is presented on 20 DEQAS samples which were analyzed by an LC-MS/MS assay developed as a candidate reference measurement procedure by the US National Institute of Standards and Technology (NIST). All 25-OHD assays should be monitored by a proficiency testing scheme and the results made available to clinicians and editors of scientific journals.

- JANSSEN M.J.W. (2012)

Multicenter comparison study of current methods to measure 25-hydroxyvitamin D in serum.
Steroids, 77:1366-72.

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25(OH)D2 in DEQAS and SRM samples was fully recognized by chromatographic methods, but only partially by protein binding and immunochemical methods. Chromatographic methods, and to a lesser extent the protein binding assay, showed cross-reactivity with 3-epi-25(OH)D3. Agreement of 25(OH)D assays to ID–LC–MS/MS in sorting patients into distinct 25(OH)D categories varied between 53% and 88%.
Significant bias exists between ID–LC–MS/MS and many, but not all, other 25(OH)D assays. The variable response among different assays for 25(OH)D metabolites impedes the use of uniform cutoff values for defining vitamin D status. Our results indicate the need towards further standardizing assays for 25(OH)D measurement.

- HEIJBOER A.C. (2012)

Accuracy of 6 Routine 25-Hydroxyvitamin D Assays: Influence of Vitamin D Binding Protein Concentration.
Clin. Chem., 58(3):543-548.

Most of the examined 25(OH)D assays showed significant deviations in 25(OH)D concentrations from those of the ID-XLC-MS/MS method. As expected, DBP concentrations were higher in samples of pregnant women and lower in samples of IC patients compared to healthy controls.
25(OH)D measurements performed with most immunoassays suffer from inaccuracies that are DBP concentration dependent. Therefore, when interpreting results of 25(OH)D measurements, careful consideration of the measurement method is necessary.

- CARTER, G.D. (2012)

25-Hydroxyvitamin D: A Difficult Analyte.
Clin. Chem., 58(3):486–488.

In summary, the studies of Farrell et al. and Heijboer et al. have identified general and specific problems in measuring 25-OHD. The standardization of 25-OHD assays is slowly being addressed, but the elimination of matrix effects, of which VDBP is an example, will require the continual vigilance of analysts and clinicians and an ongoing dialogue with manufacturers.

- HERRMANN, M. (2012)

State-of-the-Art Vitamin D Assays: A Comparison of Automated Immunoassays with Liquid Chromatography–Tandem Mass Spectrometry Methods.
Clin. Chem., 58(3):1-12.

The LC-MS/MS methods agreed. The RIA assay showed a performance comparable to LC-MS/MS. All immunoassays measured total 25OH-D (including D3 and D2), with the exception of the Roche assay (D3 only). Among the immunoassays detecting total 25OH-D, the CCCs varied between 0.85 (Abbott) to 0.95 (LIAISON). Most assays demonstrated good intra- and interassay precision, with CV10%.
Automated immunoassays demonstrated variable performance and not all tests met our minimum performance goals. It is important that laboratories be aware of the limitations of their assay.

- HEWAVITHARANA, A.K. (2013)

Recent trends in the determination of vitamin D.
Bioanal. 5(24):3063–3078.

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This review summarizes all vitamin D methods published during the 5-year period of 2008–2012. Particular emphasis has been placed on the different forms of vitamin D measured and the sample preparation procedures used in a variety of matrices. The review was divided into sections based on the typical steps of an analytical method, and the vitamin D methods were compared and critically evaluated at each step. It is hoped that the findings of this review will thus enable the reader to evaluate each stage of the analytical process and select or develop an appropriate method for their particular application. Overall, LC–MS/MS is the most common technique used within the last 5 years and it is the best option for the unambiguous identification and accurate quantification of the many different forms of vitamin D.

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3. FREE VITAMIN D

- BIKLE D.D. (1986)

Free 25-Hydroxyvitamin D Levels Are Normal in Subjects with Liver Disease and Reduced Total 25-Hydroxyvitamin D Levels.
J. Clin. Invest., 78:748-752.

Measurement of total vitamin D metabolites alone, although providing a crude assessment of vitamin D status, may not give an accurate indication of the free (biologically active) form of the vitamin. The ratio of total 25OHD3 and 1,25(OH)2D3 to plasma DBP, rather than total circulating vitamin D metabolites, may provide a more useful index of biological activity. Further studies are required to substantiate this hypothesis.

- HADDAD J.G. (1986)

Assessment of the Free Fraction of 25-Hydroxyvitamin D in Serum and Its Regulation by Albumin and the VitaminD-Binding Protein.
J. Clin. Endocrinol. Met., 63(4):954-959.

The comparison between the results obtained for 25OHD binding in serum and the results previously obtained for 1,25-(OH)2 D binding in serum showed that both vitamin D metabolites are transported in blood bound to the same proteins. The affinity constants of both DBP and albumin were 10-to20-fold higher for 25OHD than for 1,25-(OH)2 D ,but the distributions of the metabolites between DBP and albumin in normal serum were similar [88% of the 25OHD and 85% of the 1,25-(OH)2 D were bound to DBP]. Therefore, it was not surprising that the total concentrations and free fractions of 25OHD and 1,25-(OH)2 D were highly correlated to each other and to DBP and albumin concentrations in sera with a wide range of DBP and albumin concentrations. The fact that the free concentrations of 25OHD and 1,25-(OH)2 D did not correlate in these same sera suggests that the free concentrations are regulated independently and maybe a better means of assessing vitamin D status than total 25OHD and 1,25-(OH)2D concentrations, which are correlated to DBP and albumin concentrations.

- DATTA H.K. (2006)

Assessment of Vitamin D Status in Male Osteoporosis.
Clin. Chem., 52(2):248–254.

Measurement of total vitamin D metabolites alone, although providing a crude assessment of vitamin D status, may not give an accurate indication of the free (biologically active) form of the vitamin. The ratio of total 25OHD3 and 1,25(OH)2D3 to plasma DBP, rather than total circulating vitamin D metabolites, may provide a more useful index of biological activity. Further studies are required to substantiate this hypothesis.

- THADHANI R. (2010)

First trimester vitamin D, vitamin D binding protein, and subsequent preeclampsia.
Hypertension, 56(4):758-63.

Previous studies report an association between vitamin D deficiency and hypertension, including the pregnancy-specific disorder preeclampsia. Circulating vitamin D is almost entirely bound to vitamin D binding protein, which increases 2-fold during pregnancy and previous studies have not examined vitamin D binding protein or free vitamin D levels. We performed a nested case-control study within the Massachusetts General Hospital Obstetric Maternal Study, measuring first trimester total 25-

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hydroxyvitamin D (25[OH]D) and vitamin D binding protein and calculating free 25(OH)D levels. We compared these levels from pregnancies complicated by subsequent preeclampsia (cases, n=39) with those from normotensive pregnancies (controls, n=131). First trimester vitamin D binding protein and free 25(OH)D levels were similar in cases and controls and were not associated with first trimester blood pressures. These data suggest that first trimester total and free 25(OH)D levels are not independently associated with first trimester blood pressure or subsequent preeclampsia.

- HEWISON M. (2010)

LIGAND REGULATION AND NUCLEAR RECEPTOR ACTION.
Nuclear Receptors, Proteins and Cell Regulation 8, 381–417.

Collectively, these observations suggest that, like RBP, a key function of DBP is to maintain stable levels of 25OHD and/or 1,25(OH)2D in serum whilst modulating their bioavailability to peripheral tissues. More recent studies by Pike and colleagues confirmed the detrimental effect of DBP knockout on circulating levels of 1,25(OH)2D but, paradoxically, showed that target tissue levels of the steroid hormone in DBP knockout mice were no different to those in tissue from heterozygous littermates [22].

- THADHANI R. (2011)

Vitamin D–Binding Protein Modifies the Vitamin D–Bone Mineral Density Relationship.
J. Bone Miner. Res., 26(7):1609–1616.

This study provides evidence that DBP modifies the relationship between 25(OH)D and BMD in humans. Our data suggest that bioavailable 25(OH)D levels are a better of measure of vitamin D activity than total 25(OH)D levels, at least with respect to bone metabolism. It is therefore possible that by using total 25(OH)D levels as a measure of vitamin D sufficiency, individuals may be misclassified as sufficient or insufficient in vitamin D. This may explain conflicting results of prior studies of the relationship between serum 25(OH)D concentrations and BMD. Determining which individuals have a true deficit in vitamin D may allow future vitamin D supplementation interventions to be targeted to individuals most likely to benefit. Additionally, use of bioavailable 25(OH)D levels may further elucidate the nature of the relationship between vitamin D and a wide range of outcomes including fracture, infection, cancer, and cardiovascular disease.

- COYNE D.W. (2012)

Bioavailable vitamin D in chronic kidney disease.
Kidney Int., 82:5–7.

The potential effects of variable serum DBP on total versus free vitamin D metabolite levels are an important consideration in examining associations between these metabolites and various biological end points. As Bhan and colleagues demonstrate, the associations of bioavailable metabolites with calcium are significantly stronger than those of total metabolites. While further observational studies of the relationship of vitamin D levels and active vitamin D to clinical end points will undoubtedly continue to appear, clinical trials are needed to test the hypotheses that vitamin D use improves clinical outcomes.

- REESE P.P. (2012)

Changes in vitamin D binding protein and vitamin D concentrations associated with liver transplantation.
Liver Int., 32(2):287-96.

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Serum total and free 25(OH)D and DBP concentrations rose substantially following transplantation, while 1,25(OH)(2) D concentrations showed modest changes and free 1,25(OH)(2) D decreased. Studies of the effects of vitamin D status on diverse transplant complications are needed.

- HEWISON M. (2012)

Vitamin D binding protein and monocyte response to 25-hydroxyvitamin D and 1,25-dihydroxyvitamin D: analysis by mathematical modeling.
PLoS One, 7(1):e30773.

Vitamin D binding protein (DBP) plays a key role in the bioavailability of active 1,25-dihydroxyvitamin D (1,25(OH)(2)D) and its precursor 25-hydroxyvitamin D (25OHD), but accurate analysis of DBP-bound and free 25OHD and 1,25(OH)(2)D is difficult. To address this, two new mathematical models were developed to estimate: 1) serum levels of free 25OHD/1,25(OH)(2)D based on DBP concentration and genotype; 2) the impact of DBP on the biological activity of 25OHD/1,25(OH)(2)D in vivo. These novel mathematical models underline the importance of DBP as a determinant of vitamin D 'status' in vivo, with future implications for clinical studies of vitamin D status and supplementation.

- THADHANI R.I. (2012)

Bioavailable vitamin D is more tightly linked to mineral metabolism than total vitamin D in incident hemodialysis patients.
Kidney Int., 82:84–89.

This study provides additional evidence to support the notion that bioavailable, rather than total, levels of vitamin D may be more relevant measures of vitamin D status with respect to its actions on mineral metabolism. Although mineral metabolism has been the traditional focus of vitamin D actions, recent data suggest that its actions may be more widespread, with effects on the immune response, hypertension, and insulin sensitivity, among others. Studies assessing the effects of albumin and DBP in modifying these relationships will shed further light on the best way to identify individuals who are most likely to benefit from supplementation.

- SANSOM D.M. (2012)

Availability of 25-Hydroxyvitamin D3to APCs Controls the Balance between Regulatory and Inflammatory T Cell Responses.
J. Immunol., 189(11):5155-64.

An increasing body of evidence suggests that vitamin D can have profound effects on the immune system. The present data reveal that the outcome of T cell activation is strongly influenced by the availability of the inactive 25(OH)D3precursor to DCs, because, upon maturation, these cells upregulate CYP27B1 and generate local 1,25(OH)2D3 at a sufficient level for T cells to respond. Our data further suggest that the availability of 25(OH)D3depends on both the serum level of inactive 25(OH)D3and the concentration and genotype of DBP. Accordingly, the level of free vitamin D available to the immune system might be lower than that indicated by standard measures of vitamin D status but could be clinically relevant in the control of inflammatory disease.

- WEINSTEIN S.J. (2012)

Impact of circulating vitamin D binding protein levels on the association between 25-hydroxyvitamin D and pancreatic cancer risk: a nested case-control study.
Cancer Res., 72(5):1190-8.

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Taken together, our findings indicate that higher DBP concentrations may sequester more 25(OH)D and reduce free 25(OH)D bioavailability. Simultaneous examination of DBP and 25(OH)D may be important in determining the association of vitamin D with cancer risk.

- QURAISHI S.A. (2012)

Vitamin D in acute stress and critical illness.
Curr. Opin. Clin. Nutr. Metab. Care, 15(6):625-34.

Single-point assessments of 25-hydroxyvitamin D following acute stress may provide an inaccurate assessment of vitamin D status. In such cases, measurement of binding proteins and free vitamin D metabolites may be essential to create a more realistic approximation of vitamin D status. Variations in patient responses to acute stress and critical illness may depend not only on the degree of systemic vitamin D insufficiency, but also on the individual tissue requirements.

- MONDUL A.M. (2012)

British J. Cancer, 107:1589–1594.
Influence of vitamin D binding protein on the association between circulating vitamin D and risk of bladder cancer.

Our findings provide additional support for an aetiologic role for vitamin D in bladder cancer and suggest that free, rather than total, circulating vitamin D may be a more relevant exposure when examining bladder and, perhaps, other cancers.

- HEWISON M. (2013)

Measurement of 25-hydroxyvitamin D in the clinical laboratory: Current procedures, performance characteristics and limitations.
Steroids, 75(7):477-88.

In the last five years there has been revived interest in the role of DBP in Vitamin D and human health, with the target levels of serum 25OHD required for Vitamin D sufficiency being subject to much scrutiny. Based on recent studies, it is possible that free of bioavailable 25OHD will provide a more meaningful marker of Vitamin D function.

- WANG X. (2013)

Vitamin D-binding protein levels in female patients with primary hyperparathyroidism.
Endocr. Pract., 19(4):609-13.

Both serum 25(OH)D and DBP levels were lower in female patients with PHPT compared with control subjects. We suggest that a low DBP level contributes to the low 25(OH)D level observed in female PHPT patients. The etiology of the decrease in DBP and its relationship to calcium, 25(OH)D, and PTH levels require further investigation.

- MOLLER U.K. (2013)

Increased plasma concentrations of vitamin D metabolites and vitamin D binding protein in women using hormonal contraceptives: a cross-sectional study.
Nutrients, 5(9):3470-80.

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Use of hormonal contraceptives (HC) may influence total plasma concentrations of vitamin D metabolites. A likely cause is an increased synthesis of vitamin D binding protein (VDBP). Discrepant results are reported on whether the use of HC affects free concentrations of vitamin D metabolites.
In conclusion: Use of HC is associated with 13%-25% higher concentrations of total vitamin D metabolites and VDBP. This however is not reflected in indices of calcium or bone metabolism. Use of HC should be considered in the interpretation of plasma concentrations vitamin D metabolites.

- BERG I. (2013)

Vitamin D, vitamin D binding protein, lung function and structure in COPD.
Respir. Med., 107(10):1578-88.

This is the first study to demonstrate a relationship between emphysema and vitamin D. We also provide further evidence for a relationship between vitamin D and FEV1.

- GLENDENNING P. (2013)

Calculated free and bioavailable vitamin D metabolite concentrations in vitamin D-deficient hip fracture patients after supplementation with cholecalciferol and ergocalciferol.
Bone, 56:271–275.

Although cholecalciferol was more effective than ergocalciferol in increasing total 25OHD concentrations in vitamin D-deficient hip fracture patients, both calciferol formulations produced comparable increases in calculated free and bioavailable vitamin D metabolite concentrations. This might explain why cholecalciferol and ergocalciferol have similar effects on PTH. Whether the calciferol formulations are truly bioequivalent or differ in their effects on fracture and falls prevention remains to be determined in prospective comparative outcome trials.

- BIKLE D. (2013)

Variability in free 25(OH) vitamin D levels in clinical populations.
J. Steroid Biochem. Mol. Biol., S0960-0760.

Relationships between total and free 25(OH)D vary with clinical conditions that affect circulating protein concentrations, and may differ from predictions based on physiologic changes in circulating vitamin D binding protein and albumin. Direct measurement of free 25(OH) D warrants further evaluation to determine its clinical relevance in defining optimal vitamin D status for differing clinical conditions.

- DENBURG M.R. (2013)

Vitamin D bioavailability and catabolism in pediatric chronic kidney disease.
Pediatr. Nephrol., 28:1843–1853.

Winter season, older age, FSGS and GN, and higher FGF23 concentrations were independently associated with lower concentrations of free and bioavailable 25(OH)D. Black race was associated with lower total 25(OH)D and DBP, but not free or bioavailable 25(OH)D. 24,25(OH)2D was the vitamin D metabolite most strongly associated with iPTH. Lower 25(OH)D and higher iPTH concentrations, black race, and greater CKD severity were independently associated with lower levels of 24,25(OH)2D, while higher FGF23 concentrations and GN were associated with higher levels of 24,25(OH)2 D.
Children with CKD exhibit altered catabolism and concentrations of DBP and free and bioavailable 25(OH)D, and there is an important impact of their underlying disease.

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- THADHANI R. (2013)
Vitamin D–Binding Protein and Vitamin D Status of Black Americans and White Americans.
N. Engl. J. Med., 369(21):1991-2000.

Vitamin D deficiency is certainly present in persons with very low levels of total 25-hydroxyvitamin D accompanied by hyperparathyroidism, hypocalcemia, or low BMD. However, community dwelling blacks with total 25-hydroxyvitamin D levels below the threshold used to define vitamin D deficiency typically lack the accompanying characteristic alterations. The high prevalence among blacks of a polymorphism in the vitamin D–binding protein gene that is associated with low levels of vitamin D–binding protein results in levels of bioavailable 25-hydroxyvitamin D that are similar to those in whites, despite lower levels of total 25-hydroxyvitamin D. Alterations in vitamin D–binding protein levels may therefore be responsible for observed racial differences in total 25-hydroxyvitamin D levels and manifestations of vitamin D deficiency. To improve the determination of vitamin D status in diverse populations, the measurement of vitamin D–binding protein will most likely need to be incorporated into the assessment.

- BIKLE D. (2013)
Vitamin D3 effects on lipids differ in statin and non-statin-treated humans: superiority of free 25-OH D levels in detecting relationships.
J. Clin. Endocrinol. Metab., 98(11):4400-9.

Vitamin D lipid-lowering effects appear limited to statin-treated patients and are likely due to decreased cholesterol absorption. Relationships between lipids and D metabolites were only detected when free 25-OH D was measured, suggesting the superiority of determining free 25-OH D levels compared to total 25-OH vitamin D levels when analyzing biologic responses.

- YANG M. (2013)
Vitamin D-binding protein in cerebrospinal fluid is associated with multiple sclerosis progression.
Mol. Neurobiol., 47(3):946-56.

In conclusion, here we observed upregulated DBP in the cerebrospinal fluid could serve as a specific diagnostic biomarker for the progression of multiple sclerosis. Next, we demonstrate the vital function of increased levels of free vitamin D metabolites for multiple sclerosis treatment. Finally, vitamin D supplements may be particularly beneficial for SPMS patients.

- JORDE R. (2014)
Serum free and bio-available 25-hydroxyvitamin D correlate better with bone density than serum total 25-hydroxyvitamin D.
Scand. J. Clin. Lab. Invest., 74(3):177-83.

*The results of the study may have important clinical consequences. The free and/or bio-available fractions of 25(OH)D may be more strongly linked
to important biological effects than the total fraction and may be beneficial to assess for certain patient groups, such as postmenopausal females or others at risk of osteoporosis or low BMD. However, DBP is an expensive analysis. The increasing volume of 25(OH)D analyses being performed does not allow measurement and calculation of free and/or bioavailable 25(OH)D instead of total 25(OH)D for the general patient groups without a considerable cost. Genotyping of specific DBP phenotypes in order to more correctly calculate the free and/or bio-available 25(OH)D levels, would*

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increase the costs of analysis even further. In conclusion, our results indicate that free and bio-available 25(OH)D may be a more informative
measure of the vitamin D status in relation to BMD, and also that adjusting for DBP phenotype may be a further improvement. However, the findings need confirmation in larger studies.

- KARLSSON T. (2014)

Increased vitamin D-binding protein and decreased free 25(OH)D in obese women of reproductive age.
Eur. J. Nutr., 53:259–267.

Obese women had higher DBP concentrations compared with normal-weight women and lower free 25(OH)D. The obese women were more likely to have 25(OH)D concentrations that could be considered suboptimal. Vitamin D intake was generally low in normal weight and obese women of childbearing age.

- SCHWARTZ J.B. (2014)

A comparison of direct and calculated free 25(OH) Vitamin D levels in clinical populations.
J. Clin. Endocrinol. Metab., 99(5):1631-7.

Calculated free 25 (OH) D levels varied considerably from direct measurements of free 25 (OH) D with discrepancies greatest in data for African Americans. Differences in DBP binding affinity likely contributed to estimation errors between the races. Directly measured free 25-OHconcentrations were related to iPTH but calculated estimates were not. Current algorithms to calculate free 25-OH vitamin D may not be accurate. Further evaluation of directly measured free 25 (OH) D levels to determine its role in research and clinical management of patients is needed.

- RANDOLPH A.G. (2014)

Vitamin D-binding protein haplotype is associated with hospitalization for RSV bronchiolitis.
Clin. Exp. Allergy, 44(2):231-7.

Vitamin D-binding protein (VDBP) haplotypes influence free vitamin D levels. We report an association between a VDBP haplotype and hospitalization for RSV bronchiolitis in infancy in two independent cohorts.

- YOUSEFZADEH P. (2014)

Vitamin D Binding Protein Impact on 25-Hydroxyvitamin D Levels under Different Physiologic and Pathologic Conditions.
Int. J. Endocrinol., 2014:981581.

There is a high prevalence of vitamin D deficiency worldwide, but how to define vitamin D deficiency is controversial. Currently, the plasma concentration of total 25-hydroxyvitamin D [25(OH)D] is considered an indicator of vitamin D status. The free hormone hypothesis states that protein-bound hormones are inactive while unbound hormones are free to exert biological activity. The majority of circulating 25(OH)D and 1,25(OH)2D is tightly bound to vitamin D binding protein (DBP), 10–15% is bound to albumin, and less than 1% of circulating vitamin D exists in an unbound form. While DBP is relatively stable in most healthy populations, a recent study showed that there are gene polymorphisms associated with race and ethnicity that could alter DBP levels and binding affinity. Furthermore, in some clinical situations, total vitamin D levels are altered and knowing whether DBP

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is also altered may have treatment implications. The aim of this review is to assess DBP concentration in different physiological and pathophysiological conditions. We suggest that DBP should be considered in the interpretation of 25(OH)D levels.

- WANG J. (2014)

Plasma free 25-hydroxyvitamin D, vitamin D binding protein, and risk of breast cancer in the Nurses' Health Study II.
Cancer Causes Control., 25(7):819-27.

We found no association between plasma calculated free 25(OH)D and risk of breast cancer overall (highest vs. lowest quartile RR 1.21, 95 % CI 0.83-1.77, trend test p value = 0.50). No association was observed for plasma DBP as well (highest vs. lowest quartile RR 0.95, 95 % CI 0.67-1.36, trend test p value = 0.96). Results were similar by tumor hormone receptor status. Neither the total nor the calculated free 25(OH)D and breast cancer association substantially varied by plasma DBP levels.
Our study does not support an important role of either calculated circulating free 25(OH)D or circulating DBP levels in breast cancer risk among predominantly premenopausal women.

- CARTER G.D. (2014)

Assessing Vitamin D Status: Time for a Rethink?
Clin. Chem., 60(6):809–811.

The work of Powe et al. and other researchers is advancing our knowledge of vitamin D biology and the assessment of vitamin D status. The importance of accurate methods in this fundamental research, whether for 25(OH)D, VDBP, or other analytes, cannot be overstated. The potential problems of measuring 25(OH)D parallel those experienced in direct immunoassays for other steroid hormones such as testosterone. Indeed, the limitations of direct immunoassays of sex hormones were recognized in a report commissioned by the Endocrine Society.
However, robust and reliable methods for VDBP or bioavailable 25(OH)D are likely to remain elusive, with measurements confined to research laboratories for the foreseeable future. Meanwhile, when interpreting total 25(OH)D results, clinical laboratories should be mindful of possible ethnic differences in circulating VDBP. Further research is likely to lead ultimately to more meaningful measures of vitamin D status and perhaps a reassessment of the most appropriate biomarkers.

- DE PASCALE G. (2014)

Vitamin D status in critically ill patients: the evidence is now bioavailable!
Critical Care, 18:449.

We read with great interest the recent article by Amrein and colleagues demonstrating an association between 25-hydroxyvitamin D (25(OH)D) levels and adjusted hospital mortality (hazard ratio 2.05; 95% confidence interval 1.31 to 3.22). Circulating 25(OH)D levels are considered the best indicator of vitamin D status in the general population. However, 25(OH)D is predominantly bound to vitamin D binding protein in a very stable complex; indeed, only free and albumin-bound 25(OH)D may be considered available for biological functions. Formulas used to calculate the bioavailable fraction, however, were not derived from critically ill patients and may be inadequate in the ICU setting.
Hence, we strongly urge future studies related to vitamin D status in critical illness to consider incorporating direct measurements of bioavailable 25(OH)D and cathelicidin expression to further our understanding of the potential underlying biological mechanisms by which vitamin D optimization may improve ICU outcomes.

- GRONOWSKI A.M. (2015)

Vitamin D: The More We Know, the Less We Know

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Clin. Chem., 61(3):462–465.

In late 2010, the Institute of Medicine (IOM) issued a report that vitamin D supplementation was unlikely to be beneficial for any condition other than bone health and that blood concentrations of 20 ng/mL (50 nmol/L) or greater were sufficient for maintaining bone health. Since then, several metaanalyses have failed to show that low 25(OH)D concentrations are associated with risk for any of the above-mentioned nonskeletal chronic conditions, with the possible exception of fractures. Complicating the association of 25(OH)D blood concentrations with risk has been the poor agreement among 25(OH)D immunoassays (e.g., differences in recognition of 25(OH)D 2 and 25(OH)D3, the 2 forms of commercial supplements of the vitamin), for which there are ongoing efforts to standardize 25(OH)D assays. Further complicating what we know and don't know is the recent discovery of genetic polymorphisms in vitamin D binding proteins (VDBPs) that segregate well between blacks and whites, which may explain the paradox of blacks having lower 25(OH)D blood concentrations than whites but higher, or equivalent, bone density. These studies suggest that perhaps we should be looking at bioavailable 25(OH)D rather than total 25(OH)D. Here, 4 experts who have contributed to what we know about 25(OH)D address what we don't know and where we might be headed.

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4. DIASOURCE PRODUCTS REFERENCES

- FLOHR F. (2002)

Bone mineral density and quantitative ultrasound in adults with cystic fibrosis.
Eur J Endocrinol, 146(4):531-6

OBJECTIVE: With increasing life span osteoporosis becomes a more recognized problem in patients with cystic fibrosis (CF). The aim of this cross-sectional study in 75 adult patients with CF (mean age 25.3 years) was to assess the prevalence of low bone mineral density (BMD) by dual-energy x-ray absorptiometry (DEXA) and, for the first time, by quantitative ultrasound (QUS), and to identify predicting factors.
DESIGN AND METHODS: Bone status was assessed at the lumbar spine (L2-L4) and the femoral neck by DEXA, and at the calcaneus by QUS (stiffness index). These data were correlated with a variety of clinical and anthropomorphic variables. Biochemical markers of bone turnover such as osteocalcin, bone-specific alkaline phosphatase, crosslinks in urine, 25-hydroxy vitamin D (25-OH vitamin D), parathyroid hormone, calcium and free testosterone were determined by standard assays.
RESULTS: The mean BMD T score (+/-s.e.m.) was -1.4+/-0.17 at the lumbar spine, and -0.54+/-0.16 at the femoral neck. The mean T score of the calcaneal stiffness index was -0.83+/-0.19. Based on a lumbar spine T score <-2.5 by DEXA, 27% of the patients had osteoporosis. Multiple regression analysis showed that the forced expiratory volume in one second (FEV1) and the use of oral glucocorticoids were independent predictors of low lumbar spine BMD, whereas body mass index (BMI) and the use of oral glucocorticoids were independent predictors of low femoral neck BMD. The stiffness index correlated moderately with BMD (0.49-0.62, P<0.0001). QUS had a sensitivity and specificity of only 57% and 89% respectively for diagnosing 'osteoporosis' (based on a femoral neck T score <-2.5 by DEXA). Positive and negative predictive values were 36% and 95% respectively.
CONCLUSIONS: Low BMD is frequent in adults with CF and is most strongly correlated with disease severity (BMI, FEV1) and the use of glucocorticoids. Calcaneal QUS might help to screen out patients with a normal BMD, but sensitivity and specificity were not sufficiently high to replace DEXA in these patients.

25OH Vitamin D was measured with the BioSource Europe (now DIAsource) 25OH Vitamin D3 RIA assay (KIP1961).

- SHIN Y.G. (2003)

Effect of Chronic Alcohol Ingestion on Bone Mineral Density in Males without Liver Cirrhosis.
The Korean Journal of Internal Medicine, 18:174-180

Background : Osteoporosis in men is an important public health problem. Because of the tendency of the numbers of the elderly population to increase, and age-specific incidence of fractures, it is inevitable that the health burden due to fractures will increase. Chronic alcoholism is associated with other risk factors, such as poor nutrition, leanness, liver disease, malabsorption, vitamin D deficiency, hypogonadism, hemosiderosis, parathyroid dysfunction and tobacco use, and these may contribute to the pathogenesis of bone disease related to alcoholism. Chronic alcohol intake may reduce bone density, but can also increase bone density. It is well established that liver disease also induces bone density changes, thus it is difficult to distinguish the role of liver disease from that of alcohol itself in the bone alterations occurring in patients with chronic alcohol consumption. Chronic male alcoholics, not having liver cirrhosis were studied to assess the effect of chronic alcohol consumption on their bone mineral density.
Methods : The study subjects comprised of 18 chronic heavy drinkers of more than 40 g of alcohol per day for at least 3 years and 18 age-matched controls who drank less than 20 g of alcohol per day. The serum and urinary parameters of bone and mineral metabolism were determined. The bone mineral

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density (BMD) was measured by dual-energy X-ray absorptiometry at four axial sites (lumbar spine, femoral neck, Ward's triangle and trochanter).
Results : The alcoholic and control patients drank an average of 97.6 g and 7.2 g of alcohol per day. Osteocalcin, a marker of bone formation, was slightly decreased in alcoholic patients, and deoxypyridinoline, a marker of bone resorption, was slightly increased, but the difference was not statistically significant (p>0.05). There were no differences between the two groups in the levels of free testosterone, estradiol, 25(OH) vitamin D and parathyroid hormone. The Ward's triangle and trochanter BMDs of the femur were significantly lower in the alcoholics than the controls, and lumbar spine BMD was decreased in proportion to the total alcohol intake in the alcoholics (r=-0.625, p=0.01).
Conclusion : We suggest that chronic alcohol consumption induces low bone density in the femur Ward's triangle and trochanter. There was also a significant inverse correlation between the lumbar spine BMD and the total amount of alcohol consumed. Large scaled randomized and prospective studies are needed to clarify the pathogenesis of alcohol linduced osteoporosis.

25OH Vitamin D was measured with the BioSource Europe (now DIAsource) 25OH Vitamin D3 RIA assay (KIP1961).

- MALYSZKO J. (2003)

Osteoprotegerin and its correlations with new markers of bone formation and bone resorption in kidney transplant recipients.
Transplant Proc, 35(6):2227-9

Osteoprotegerin (OPG), a natural decoy receptor for osteoclast differentiation factor, is produced by osteoblasts in response to PTH. OPG and its ligand RANKL constitute a complex mediator system involved in the regulation of bone resorption, probably playing an important role in the homeostasis of bone turnover. At present, little is known about the effects of OPG on uremic bone. Successful kidney transplantation reverses many abnormalities of bone metabolism; however, the improvement is often incomplete. The aim of the study was to assess OPG and RANKL concentrations in long-term kidney allograft recipients and their correlations with biochemical markers of bone resorption and formation. The present studies on 48 kidney transplant recipients and 25 healthy volunteers included concentrations of parathormone, osteocalcin, bone-specific alkaline phosphatase, serum CrossLaps, calcidiol, calcitriol, ICTP, PICP, tartrate-resistant acid phosphatase, beta2 microglobulin, IGF-1, IFGBP-1, IGFBP-3, OPG, and RANKL using commercially available kits for measurements. Among kidney transplant recipients OPG and RANKL did not differ between transplant patients and healthy volunteers, whereas other markers of bone formation and resorption were significantly higher in the former group. OPD was related to age, time on dialysis prior transplantation, urea, platelet count, CSA dose, azathioprine dose, 25(OH)D(3), TRAP, IGF-1, IGFBP-3, whereas RANKL was related to leukocyte count, CSA concentration and dose, urine DPD, and beta2 microglobulin content. In healthy volunteers OPG correlated only with CrossLaps, whereas RANKL correlated only with osteocalcin and TRAP. Correlations between OPG, IGF system components, and some markers of bone metabolism may indicate the role of OPG/RANKL system in the pathogenesis of bone metabolism disturbances following renal transplantation.

25OH Vitamin D and 1,25$(OH)_2$ Vitamin D were measured respectively with the BioSource Europe (now DIAsource) 25OH Vitamin D3 RIA assay (KIP1961) and 1,25$(OH)_2$ Vitamin D RIA assay (KIP1929).

- KYUNG SUNG I. (2004)

Effects of Insulin-like Growth Factor-I and 1,25-(OH)2 Vitamin D3 Concentration on Intrauterine Growth of Newborns from Mothers with Preeclampsia.
Korean Journal of Pediatrics, 47(5), 527-531

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Purpose : This study was undertaken to observe the blood levels of IGF-I and 1,25-(OH)2 Vit. D3 in maternal and neonatal compartments and the effects of IGF-I concentration on intrauterine fetal growth and 1,25-(OH)2 Vit. D3 metabolism in the presence of preeclampsia.
Methods : Thirty-four full-term pregnant women with preeclampsia and their newborns (preeclampsia group) and 10 normotensive full-term pregnant women and their newborns(normotensive group) were observed. IGF-I and 1,25-(OH)2 Vit. D3 concentrations in maternal and umbilical cord blood were analyzed.
Results : Maternal and umbilical cord blood levels of IGF-I and 1,25-(OH)2 Vit. D3 were significantly lower in the preeclampsia group than in the normotensive group. In the preeclampsia group, maternal and cord blood levels of IGF-I of small-for-gestational age newborns were significantly lower than those of appropriate-for-gestational age newborns. The birth weight and length of newborns correlated with IGF-I concentrations of maternal and umbilical cord blood in small-for-gestational age newborns of preeclampsia group. The correlation between IGF-I and 1,25-(OH)2 Vit. D3 was significant in the umbilical cord blood of preeclampsia group, but only in appropriate-for-gestational age newborns.
Conclusion : It is suggested that the lower level of IGF-I is the primary factor of intrauterine growth retardation in preeclampsia, and the effect of IGF-I on the metabolism of 1,25-(OH)2 Vit. D3 is different according to the presence of preeclampsia and intrauterine fetal growth retardation.

$1,25(OH)_2$ Vitamin D was measured with the BioSource Europe (now DIAsource) $1,25(OH)_2$ Vitamin D RIA assay (KIP1929).

- POLAK-JONKISZ D. (2004)

Vitamin d3 metabolites in children with end-stage renal failure.
Przegl¥d pediatryczny, 34(1):42

The active vitamin D metabolite production disturbances in progressive renal insufficiency lead to renal osteodystrophy. The aim of the present study was to estimate the serum levels of 1.25-dihydroksycholekalciferol (1.25(OH)2D3) and 25- hydroksycholekalciferol (25(OH)D3) in correlation with parathyroid function and mineral bone density in children with end-stage renal disease. The study comprised children aged 5-18 years who were divided into 2 groups: I - 16 healthy children, II - 16 CRF patients on hemodialysis or ADO treated with alphacalcidol. Intact parathormon (iPTH), 1.25(OH)2D3, 25(OH)D3, calcium (Ca), and phosphate (P) serum levels were measured. Densitometry was performed by Lunar DPX-L system and the skeleton has been investigated (TB). Results: iPTH hypersecretion was accompanied by statistically significant hyperphosphatemia. Serum calcium levels were lower than in healthy children although they didn't reach the significance level. Mean vitamin D metabolite values were comparable with those in the control group, although 1.25(OH)2D3 concentrations were slightly lower. Conclusions: 1. Even slightly decreased 1.25(OH)2D3 serum concentrations lead to iPTH hypersecretion in dialysed children. 2. Renal osteodystrophy in this group may appear despite alfakalcidol supplementation.

25OH Vitamin D and $1,25(OH)_2$ Vitamin D were measured with respectively the BioSource Europe (now DIAsource) 25OH Vitamin D3 RIA assay (KIP1961) and $1,25(OH)_2$ Vitamin D RIA assay (KIP1921, now KIP1929).

- PANIDIS D. (2005)

Serum Parathyroid Hormone Concentrations Are Increased in Women with Polycystic Ovary Syndrome.
Clin. Chem., 51(9):1691–1697

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Background: The present study was designed to investigate the effects of polycystic ovary syndrome (PCOS) and of obesity on serum parathyroid hormone (), 25-hydroxyvitamin D (25-OH-vitamin D), and 1,25-dihydroxyvitamin D [1,25-(OH)2-vitamin D] concentrations and the possible associations of the above calciotropic hormones with the hormonal and metabolic characteristics of the syndrome.
Methods: We studied 58 obese [body mass index (BMI) >30 kg/m2] women with PCOS, 64 overweight (I, 25–30 kg/m2) women with the syndrome, 169 normal weight (BMI <25 kg/m2) women with PCOS, 29 obese controls (ovulatory women without clinical or biochemical hyperandrogenemia), 14 overweight controls, and 70 normal-weight controls. Blood samples were collected (at 0900 after an overnight fast) between the 3rd and 6th days of a menstrual cycle in the control groups and during a spontaneous bleeding episode in the PCOS groups. Circulating concentrations of luteinizing hormone (LH), follicle-stimulating hormone (FSH), prolactin (PRL), testosterone, 4-androstenedione, 17-hydroxyprogesterone, sex-hormone–binding globulin (SHBG), insulin, glucose, PTH, 25-OH-vitamin D, and 1,25-(OH)2-vitamin D were measured.
Results: Both PCOS and increased body weight had a significant positive effect on serum PTH values. PTH concentrations were significantly correlated with age, BMI, glucose, PRL, SHBG, and testosterone. Only the correlations with testosterone and PRL were BMI-independent. The effect of PCOS on PTH concentrations remained significant after adjustment for BMI, but not after adjustment for testosterone concentration. Increased body weight also had a significant negative effect on 25-OH- and 1,25-(OH)2-vitamin D concentrations, but no association with the syndrome was observed.
Conclusions: The results of the present study are in agreement with previous data supporting an association of increased PTH and decreased vitamin D metabolite concentrations with obesity. Moreover, the present findings indicate, for the first time, that PTH probably is also linked to PCOS-associated hyperandrogenism.

25OH Vitamin D and $1,25(OH)_2$ Vitamin D were measured with respectively the BioSource Europe (now DIAsource) 25OH Vitamin D3 RIA assay (KIP1961) and $1,25(OH)_2$ Vitamin D RIA assay (KIP1921, now KIP1929).

- BERK F. (2005)

Subclinical Vitamin D Deficiency Is Increased in Adolescent Girls Who Wear Concealing Clothing.
J. Nutr., 135:218–222

Vitamin D deficiency continues to be a worldwide problem, especially in developing countries. The aim of this study was to investigate potential risk factors for vitamin D deficiency. Girls (n 89) aged 13 to 17 y were enrolled in the study. Study subjects were stratified into 3 groups: Group I included girls living in a suburban area; Group II girls lived in an urban area, and Group III girls lived in an urban area and wore concealing clothes for religious reasons. At the end of winter (in April) serum 25-hydroxyvitamin D [25(OH)D] levels were measured and dietary data were collected using questionnaires. Vitamin D deficiency was defined as a serum 25(OH)D concentration 25 nmol/L, and insufficiency as a 25(OH)D concentration between 25 and 50 nmol/L. The lumbar and femur neck bone mineral densities (BMD) were measured using dual X-ray absorptiometry (DEXA). Overall, 39 girls (43.8%) had vitamin D insufficiency and 19 (21.3%) had vitamin D deficiency. In group III (wearing covered dress) the serum 25(OH)D concentrations (28.13 12.53 nmol/L) were significantly lower than in the other 2 groups, and within this group, 50% of girls were vitamin D deficient. The lumbar and femur neck BMD of girls with lower 25(OH)D levels did not differ from those with adequate vitamin D levels. We conclude that vitamin D deficiency is an important problem in Turkish adolescent girls, especially in those who follow a religious dress code; therefore, vitamin D supplementation appears to be necessary for adolescent girls.

25OH Vitamin D was measured with the BioSource (now DIAsource) 25OH Vitamin D3 RIA assay (KIP1961).

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- ATLI T. (2005)

The prevalence of Vitamin D deficiency and effects of ultraviolet light on Vitamin D levels in elderly Turkish population.
Arch Gerontol Geriatr, 40(1):53-60

Vitamin D deficiency is commonly found in the elderly and is associated with osteoporosis and hip fractures. In this study, Vitamin D status of 138 female and 87 male subjects living in old age homes (OAH) and 171 female and 24 male subjects living in own homes (OH) from Central Anatolia were assessed. A questionnaire was applied to collect information about wearing features and degree of sunlight exposure and benefiting from ultraviolet index calculated (BFUI). We have found Vitamin D deficiency in 33.4% among our subjects. Also, 40.1% of subjects living in OAH (54.1% of females and 18.4% of males) and 24.4% of subjects living in OH (27.9% of females and 4.2% of males) were Vitamin D deficient. Vitamin D deficiency was significantly higher in subjects living in OAH than subjects living in OH (P = 0.001) and also higher in females than males (40.7% versus 15.3%, P < 0.001). Subjects with Vitamin D deficiency were older (P < 0.001), BFUI was lower (P < 0.001) and parathyroid hormone (PTH) was higher (P < 0.001) than those having normal level of 25(OH)D. There was a significant negative correlation between 25(OH)D levels and age (P < 0.001, r = -0.248) PTH and 25(OH)D (P = 0.004, r = -0.340), and positive correlation between 25(OH)D and BFUI (P < 0.001, r = 0.340). Vitamin D deficiency is very common in Turkish elderly subjects especially living in OAH and there is a significant low exposure to sunlight among them. Simply by asking clothing habits and exposure to sunlight, we can able to identify risk of Vitamin D insufficiency in elderly subjects.

25OH Vitamin D was measured with the BioSource (now DIAsource) 25OH Vitamin D3 RIA assay (KIP1961).

- ORBAK Z. (2005)

Rickets in early infancy: the characteristic features.
Çocuk Saðlýðý ve Hastalýklarý Dergisi, 48:8-13

Rickets in early infancy is mostly due to maternal vitamin D deficiency. Infants in this period do not present with typical biochemical and radiologic features and are difficult to diagnose. In this study, it was aimed to evaluate the characteristic features of 42 cases diagnosed as early rickets and to stress hyperphosphatemia at admission. Risk factors for vitamin D deficiency, clinical and biochemical characteristics at admission and parathyroid hormone (PTH) responses of 42 cases (27 boys, 15 girls), who were diagnosed as rickets in the first three months of life, were evaluated cross-sectionally. Mean age of the infants was 60 ± 19 (range: 32 to 112) days. Thirty-three cases (78.7%) presented with convulsion, while seven infants (16.7%) were admitted with respiratory symptoms. The serum 25-OHD levels, which could be measured in 29 infants and 15 mothers, were very low. Though all infants' serum calcium levels were low, only 26 infants (68%) presented with secondary hyperparathyroidism. Fourteen patients (35%) had high serum phosphorus levels at diagnosis. Seventy-nine percent of all mothers covered their heads outside the home, did not work and spent most of their time indoors. None of the mothers were reported as having used any vitamin D preparations during pregnancy and none of the babies was receiving vitamin D supplement. Infants of mothers at risk for vitamin D deficiency should receive vitamin D support, otherwise they present with symptoms of vitamin D deficiency in the first three months of life. Although hypocalcemia is prominent in these babies, serum PTH does not reach expected levels. Because of the immaturity of the regulating factors of PTH and serum calcium, these infants often present with hypocalcemia due to the failure of progression of disease from stage 1 to stage 2. Therefore, serum phosphorus levels may be high at admission. Because maternal vitamin D deficiency is frequently observed in our country, hypocalcemia in early infancy should usually alert the physician to deficiency of vitamin D.

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25OH Vitamin D was measured with the BioSource (now DIAsource) 25OH Vitamin D3 RIA assay (KIP1961).

- PATIÑO-GARCIA A. (2006)

Bone Mineral Density and Bone Metabolism In Children Treated for Bone Sarcomas.
Pediatric Research, 59:866–871

In adolescent bone sarcoma patients, bone mass acquisition is potentially compromised at a time in which it should be at a maximum. To evaluate the problem we measured bone mineral density (BMD) and serum markers of bone formation and resorption in a series of pediatric patients with bone tumors. BMD was measured by dual-energy x-ray absorptiometry, at clinical remission, for lumbar spine and the neck of the femur in 38 osteosarcoma and 25 Ewing's sarcoma patients. Mean age was 20.65 and 19.13 y respectively. Serum markers of bone metabolism were: OC, PICP, ICTP, 25-OH vit D and 1,25-(OH)2 vit D, IGF-I, IGFBP-3 and intact PTH. Serum was sampled throughout anti-tumoral treatments and follow-up. We analyzed 85 samples from 59 osteosarcoma patients and 54 samples from 36 Ewing's sarcoma patients. Patients had decreased lumbar and femoral BMD. The decrease was more pronounced in pubertal patients compared with those who had completed pubertal development at the time of disease diagnosis. Multivariate analysis indicated that sex, age, weight and BMI were significant in lumbar BMD depletion. Weight and BMI were significant in femoral BMD depletion. Serum markers of bone formation (PICP and OC) and resorption (ICTP) were, throughout, lower than reference values. Significant alterations in other markers were also observed. Up to a third of osteosarcoma and Ewing's sarcoma patients in clinical remission had some degree of BMD deficit. The corresponding increased risk of pathologic bone fractures constitutes a reduction in future quality of life.

25OH Vitamin D and 1,25$(OH)_2$ Vitamin D were measured with respectively the BioSource Europe (now DIAsource) 25OH Vitamin D3 RIA assay (KIP1961) and 1,25$(OH)_2$ Vitamin D RIA assay (KIP1921, now KIP1929).

- GIANOTTI L. (2006)

A slight decrease in renal function further impairs bone mineral density in primary hyperparathyroidism.
J Clin Endocrinol Metab, 91(8):3011-6

BACKGROUND: The impairment of renal function can affect the clinical presentation of primary hyperparathyroidism (PHPT), increasing cardiovascular morbidity, fracture rate, and the risk of mortality.
AIM: The aim of the study was to assess the differences in bone status in a series of consecutive patients affected by PHPT without overt renal failure at diagnosis grouped according to creatinine clearance (Ccr).
METHODS: A total of 161 consecutive patients with PHPT were studied. They were divided into two groups based on Ccr. Group A had Ccr 70 ml/min or less (n = 49), and group B had Ccr greater than 70 ml/min (n = 112). PTH, total and ionized serum calcium; urinary calcium and phosphate; serum 25-hydroxyvitamin D3; serum and urinary bone markers; lumbar, forearm, and femoral bone mineral density (BMD) were evaluated.
RESULTS: Patients in group A were older than those in group B (P < 0.0001). PTH levels did not differ in the two groups, whereas both urinary calcium and phosphorus were lower in group A than group B (P < 0.01). Lower BMD was evident in group A at lumbar spine (P < 0.002), forearm (P < 0.0001), and femur (P < 0.01). In asymptomatic PHPT, those with Ccr 70 ml/min or less had lower forearm BMD than patients with higher Ccr (P < 0.00001). When adjusting for age and body mass index in PHPT,

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BMD at each site persisted being lower (P < 0.05) in group A than group B. In all PHPT subjects, Ccr (beta = 0.29, P < 0.0005), age (beta = -0.27, P < 0.00001), and PTH levels (beta = -0.27, P < 0.0005) were all independently associated with forearm BMD.
CONCLUSIONS: In PHPT a slight decrease in renal function is associated with more severe BMD decrease, independent of age, body mass index, and PTH levels. This association is also present in asymptomatic PHPT and strengthens the National Institutes of Health recommendations for surgery in patients with mild PHPT.

25OH Vitamin D was measured with the BioSource Europe (now DIAsource) 25OH Vitamin D3 RIA assay (KIP1961).

- ABDEL-HALIM M.R.E. (2006)

Skin and serum levels of calcium, phosphorus and vitamin D3 in uremic pruritus patients before and after broad band ultraviolet B (UVB) phototherapy.
Egyptian Dermatology Online Journal, 1(2):1

Background: Pruritus is one of the commonest frustrating manifestations in chronic renal failure. The exact cause of uremic pruritus is unknown and several factors are reported to be involved in its pathogenesis, the most important of which are abnormalities in calcium and phosphorus metabolism. Broad band UVB phototherapy plays an important role in treatment of uremic pruritus through different mechanisms.
Aim of work: The aim of this work was to evaluate skin and serum levels of calcium and phosphorus and their regulating hormone, vitamin D in uremic patients before and after broad band UVB phototherapy to verify their role in the pathogenesis of uremic pruritus.
Patients and Methods: The study included 18 patients of uremic pruritus and 9 controls. A 4 mm punch biopsy and 5cm blood sample were taken from all patients before and after UVB phototherapy (when patients reported clinical disappearance of itching). Similar samples were taken from controls before the start of the study.
Results: The serum and skin calcium in uremic patients before UVB phototherapy were lower than the controls, and they increased significantly after phototherapy. The serum levels of calcium were normalized after phototherapy. On the other hand, though the skin content of calcium was increased significantly after phototherapy, it was still significantly less than controls. The serum phosphorus in uremic patients before UVB phototherapy was higher than the controls, and it decreased significantly after UVB phototherapy, though it remained significantly higher than controls. On the other hand, skin content of phosphorus in uremic patients before UVB phototherapy was less than in controls, and it decreased significantly after UVB phototherapy. Serum and skin contents of vitamin D in uremic patients increased significantly after UVB phototherapy.
Conclusion: It appears from this study that hyper- or hyperphosphatemia may represent a circulating pruritogenic substance that stimulates itching pathways in uremic patients. In addition, we postulate that hypocalcaemia and low skin calcium content, together with the previously reported disrupted calcium ion gradient, may have a direct relation to the stimulation of itching pathways. The main role of UVB in improving pruritus may be related to its systemic normalizing effect on both calcium and phosphorus (increasing calcium and lowering phosphorus).

$1,25(OH)_2$ Vitamin D was measured with the BioSource Europe (now DIAsource) $1,25(OH)_2$ Vitamin D RIA assay (KIP1929).

- TEKGUL H. (2006)

Bone Mineral Status in Pediatric Outpatients on Antiepileptic Drug Monotherapy.
Journal of Child Neurology, 21(5):411

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Drug-induced osteopenia has been reported in institutionalized children on chronic antiepileptic drug therapy. The aim of this study was to assess longitudinally bone mineral status in pediatric outpatients on antiepileptic drug monotherapy. The study group consisted of 30 ambulatory children on a normal diet: 15 on valproic acid, 11 on carbamazepine, and 4 on phenobarbital monotherapy. Bone mineral density, serum active vitamin D (1,25-dihydroxyvitamin D), and certain biochemical markers of bone formation (calcium, phosphorus, alkaline phosphatase, intact parathyroid hormone, osteocalcin, calcitonin, and urinary calcium to serum creatinine and urinary phosphorus to serum creatinine ratios) were studied at the beginning of antiepileptic drug monotherapy and at the end of 2 years of treatment. Age- and sex-specific Z-scores of bone mineral density were measured at anterior-posterior L2–L4 by dual-energy x-ray absorptiometry. Drug induced osteopenia was defined in only two patients (one on carbamazepine and the other on phenobarbital monotherapy), with Z-scores of bone mineral density less than –1.5. Serum levels of active vitamin D and biochemical markers were not significantly correlated with the Z-scores of bone mineral density. We detected a frequency of antiepileptic drug–induced osteopenia of 6.7% in pediatric outpatients after 2 years of monotherapy. However, osteopenia was not attributed to a defect in serum active vitamin D production owing to hyperparathyroidism in children on antiepileptic drug monotherapy.

1,25$(OH)_2$ Vitamin D was measured with the BioSource Europe (now DIAsource) 1,25$(OH)_2$ Vitamin D RIA assay (KIP1929).

- LARIJANI B. (2007)

Vitamin D status in mothers and their newborns in Iran.
BMC Pregnancy and Childbirth, 7:1

Background: Adequate vitamin D concentrations during pregnancy are necessary to neonatal calcium homeostasis, bone maturation and mineralization. The aim of study is to evaluate serum vitamin D concentrations in mothers and their newborns and effect of vitamin D deficiency on pregnancy outcomes.
Methods: 552 pregnant women were recruited from Tehran University educating hospitals in the winter of 2002. Maternal and cord blood samples were taken at delivery. The serum was assayed for 25-hydroxyvitamin D3, calcium, phosphorus and parathyroid hormone.
Results: The prevalence of vitamin D deficiency in maternal and cord blood samples were 66.8% and 93.3%, respectively (<35 nmol/l). There was significant correlation between maternal and cord blood serum concentrations of vitamin D. In mothers with vitamin D deficiency, cord blood vitamin D concentrations was lower than those from normal mothers (P = .001). Also, a significant direct correlation was seen between maternal vitamin D intake and weight gain during pregnancy.
Conclusion: Consideration to adequate calcium and vitamin D intake during pregnancy is essential. Furthermore, we think it is necessary to reconsider the recommendation for vitamin D supplementation for women during pregnancy.

25OH Vitamin D was measured with the BioSource Europe (now DIAsource) 25OH Vitamin D3 RIA assay (KIP1961).

- ERBIL Y. (2007)

Predictive Value of Age and Serum Parathormone and Vitamin D3 Levels for Postoperative Hypocalcemia After Total Thyroidectomy for Nontoxic Multinodular Goiter.
Arch. Surg., 142(12):1182

Hypothesis: Age, postoperative serum parathormone (PTH) level, and preoperative serum 25-hydroxyvitamin D3 (25-OHD) level predict postoperative hypocalcemia after total thyroidectomy.

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Design: Prospective clinical trial.
Setting: Tertiary referral center.
Patients: One hundred thirty patients with nontoxic multinodular goiter. Patients were divided into 2 groups according to the postoperative serum calcium level. Group 1 (n=32) consisted of patients with a postoperative serum calcium level of 8 mg/dL or less, and group 2 (n=98) consisted of patients with a postoperative serum calcium level higher than 8 mg/dL.
Interventions: The preoperative serum 25-OHD level and preoperative and postoperative serum calcium and PTH levels were determined.
Main Outcome Measures: The number of patients developing hypocalcemia and prediction of postoperative hypocalcemia by the serum 25-OHD and PTH levels.
Results: Hypocalcemia developed in 32 patients (24.6%) (group 1). The preoperative serum 25-OHD level and postoperative serum calcium and PTH levels in group 1 were significantly lower than in group 2 (P=.001). With logistic regression analysis, factors that were predictive of postoperative hypocalcemia included a preoperative serum 25-OHD level less than 15 ng/mL (P.001; odds ratio, 558.5), a postoperative serum PTH level less than 10 pg/mL (P=.01; odds ratio, 16.4), and being older than 50 years (P=.01; odds ratio, 4.6).
Conclusions: Age, a low preoperative serum 25-OHD level, and a low postoperative serum PTH level are significantly associated with postoperative hypocalcemia. The low preoperative serum 25-OHD level was more significant than the low postoperative serum PTH level in the prediction of postoperative hypocalcemia.

25OH Vitamin D was measured with the BioSource Europe (now DIAsource) 25OH Vitamin D3 RIA assay (KIP1961).

- CRAVER L. (2007)

Mineral metabolism parameters throughout chronic kidney disease stages 1–5—achievement of K/DOQI target ranges.
Nephrol. Dial. Transplant., 22:1171–1176

Background. Dialysis Outcomes and Practice Patterns Study has shown that the proportion of haemodialysis patients with adequate mineral metabolism parameters according to the Kidney Disease Outcome Quality Initiative (K/DOQI) guidelines is very low. The adequacy of such parameters in relation to the recommended ranges in patients with different chronic kidney disease (CKD) stages has not been reported. The objective of this study is to provide an in-depth description of mineral metabolism in the early stages of CKD in a European population, and to compare it with current recommendations for stages 3–5 (K/DOQI guidelines).
Methods. A total of 1836 patients were classified into stages 1–5 according to K/DOQI guidelines. The following clinical and biochemical data were recorded: age, gender, CKD aetiology, presence of diabetes, serum creatinine, creatinine clearance, serum phosphate, calcium, Ca P product and intact parathyroid hormone (PTH).
Results. A decrease in 1,25-dihydroxyvitamin D and an increase in PTH are the earliest mineral metabolism alterations in CKD, while serum calcium and phosphate are altered later in the course of CKD. The percentages of patients with serum levels within the recommended K/DOQI guidelines for stages 3, 4 and 5 were as follows: serum calcium: 90.7, 85.6 and 55; serum phosphate: 90.9, 77.1 and 70.3; iPTH 42.4, 24.6 and 46.8 and Ca P product 99.9, 99.6 and 83.8, respectively. The percentages of patients who had all four parameters within the recommended ranges were 34.9, 18.4 and 21.6 for stages 3, 4 and 5, respectively.
Conclusion. Mineral metabolism disturbances start early in the course of CKD. The first alterations to take place are a 1,25-dihydroxyvitamin D decrease, a 24 h urine phosphate decrease and a PTH elevation, which show significant level variation when the glomerular filtration rate falls below 60 ml/min. K/DOQI recommended levels for mineral metabolism parameters are difficult to accomplish, in particular for PTH levels.

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25OH Vitamin D was measured with the BioSource (now DIAsource) 25OH Vitamin D3 RIA assay (KIP1961).

- MAI K. (2007)

Interaction between vitamins A and D on growth and metabolic responses of abalone Haliotis discus hannai, Ino.
Journal of Shellfish Research

A 152-day growth experiment was conducted in a recirculated water system to investigate the interaction between vitamins A (retinol) and D (cholecalciferol) on growth and metabolic responses in abalone Haliotis discus hannai Ino. Triplicate groups of juvenile abalone (initial weight: 0.35 [+ or -] 0.03 g; initial shell length: 11.31 [+ or -] 0.25 mm) were fed to satiation one of 16 semipurified diets containing 0, 1 x [10.sup.3], 1 x [10.sup.5], 1 x [10.sup.6] IU/kg vitamin A and 0, 500, 1 x [10.sup.3], 5 x [10.sup.3] IU/kg vitamin D in a 4 x 4 factorial design. Abalone were weighed and shell-length measured on the 76th day and the 152nd day, respectively. The total specific growth rate (SGR) during the 152 days, neither the SGR in the first 76 days nor in the second 76 days, was significantly influenced by the interaction between vitamins A and D. Dietary vitamins A and D significantly stimulated viscera 25-hydroxyvitamin [D.sub.3] [25(OH)[D.sub.3]] and 1[alpha],25-dihydroxyvitamin [D.sub.3] [1[alpha],25[(OH).sub.2][D.sub.3]] contents in a cooperative fashion. Dietary vitamin A generally increased the alkaline phosphatase (AKP) activity in viscera except the excessive supplement(1 x [10.sup.3] IU/kg), which significantly decreased AKP activity. Dietary vitamin D significantly increased AKP activity. Contents of P, not Ca and Mg, in soft body increased with dietary vitamin D supplement. Dietary vitamin A significantly improved contents of lipid and retinol in soft body and viscera, respectively. Meanwhile, dietary vitamin D significantly increased contents of ash and cholecalciferol in soft body and viscera, respectively. Based on these results, interaction between vitamins A and D was expressed in various manners as different indicators were considered, though there was potential antagonism mechanism at molecular level between the two fat-soluble vitamins.

25OH Vitamin D and 1,25$(OH)_2$ Vitamin D were measured with respectively the BioSource Europe (now DIAsource) 25OH Vitamin D3 RIA assay (KIP1961) and 1,25$(OH)_2$ Vitamin D RIA assay (KIP1929).

- TEISSEYRE J. (2007)

Bone mineral metabolism in children with biliary atresia after living related liver transplantation. Evaluation of selected parameters.
Ann. Transplant., 12(2):19-25

Background: Aim of the study was to analyze the effect of living related liver transplantation on selected parameters of bone formation and resorption in children with liver cirrhosis caused by biliary atresia.
Material/Methods: 20 children (13F/7M) with biliary atresia aged from 6 month to 2.4 years were enrolled into the study 4–9 days before liver transplantation. Osteocalcin, procollagen 1 aminoterminal propeptide, collagen type 1 crosslinked C-telopeptide, parathyroid hormone and metabolites of vitamin D: 25(OH)D3 , 1,25(OH)2 D3 were measured before, 3, 6 and 12 months after liver transplantation.
Results: Three months after living related liver transplantation statistically significant increase of osteocalcin, collagen type 1 crosslinked C-telopeptide, parathyroid hormone and 1,25(OH)2 D3 levels were found. We didn't observe further increase of these parameters during the next 9 months after liver transplantation. There was no difference in 25(OH)D3 levels in patients before and after liver transplantation.

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Conclusions: In children after successful living related liver transplantation we observed improvement of selected parameters of bone formation and resorption which indicate stimulation of growing processes and mechanisms of bone geometry modelling.

$1,25(OH)_2$ Vitamin D was measured with the BioSource (now DIAsource) $1,25(OH)_2$ Vitamin D RIA assay (KIP1929).

- LARIJANI B. (2008)

Normative Values of Vitamin D Among Iranian Population: A Population Based Study.
International Journal of Osteoporosis and Metabolic Disorders, 1:8-15

There is no agreement about normal level of vitamin D and its deficiency stages. For finding normative value of Vitamin D and evaluating the state of vitamin D level in Iranian population we revised the data that was collected in Iranian national Multi-center Osteoporosis Study (IMOS). We chose 5 cities with different climates; individuals were selected by random cluster sampling. Healthy people aged 20-69 were entered into the study and serum vitamin D and PTH levels were measured. We stratified subjects based on their vitamin D levels in 7 groups and compared mean PTH levels of adjacent groups. We evaluated 5329 blood samples for vitamin D and PTH and found three steps of PTH elevation with decreasing vitamin D levels for women (40, 25 and 12 nmol L-1) and two (35 and 25 nmol L-1) for men. We use these values as cutoff levels for definition of normal, mild, moderate and severe vitamin D deficiency states. Based on these cutoffs, prevalence of all stages of vitamin D deficiency was unexpectedly high in all cities. Vitamin D deficiency state was seen in 75.1% of women and 72.1% of men. The high prevalence of vitamin D deficiency in Iran is similar to the results of other studies in Middle East area and indicates a need for a careful search for a determination of cause and need for regular fortification program.

25OH Vitamin D was measured with one of the BioSource (now DIAsource) 25OH Vitamin D RIA assay (KIP1961 or KIP1971).

- KIM Y.S. (2008)

Dietary Calcium Intake and Bone Metabolism in Korean Postmenopausal Women.
Korean Journal of Bone Metabolism, 15(2):143-149

Objective: There is a consensus that adequate calcium intake helps to prevent bone resorption and osteoporosis especially in person with low calcium diets. Even though people are concerned about bone health and are encouraged to take calcium supplementation, we believe that most people do not have enough calcium in their diets. The purpose of this study was to determine the nutritional status, urine calcium, bone markers and their relationship in Korean postmenopausal women.
Subjects: The subjects were 56 healthy female with postmenopausal osteopenia and osteoporosis (mean age, 57.7 years). Dietary calcium, phosphorus and protein were measured by 24 hrs recall method and urine calcium, bone markers, 25-OH D were measured in the fasting state.
Results: The mean (SD) daily dietary intakes of Ca, P, protein were 616 (211.9) mg, 1002 (258.6) mg, 64.8 (16.7) g respectively. Only 6.5% of the participants had calcium intake of more than 1000 mg. 55.4% of the subjects showed 25-OH D of less than 30 ng/ml. The subjects showing hypercalciuria were 29.1%. Multiple regression analysis showed that urinary calcium excretion was associated with serum P, CTX, 25-OH D but not calcium intake. The mean value of 24 hr-urine calcium was 0.22 g and it was significantly decreased into 0.18 g after 6 month supplementation of 500 mg of elemental calcium and 400 IU of vitamin D. 57.2% of the hypercalciuric subjects showed normocalciuria after supplementation. An average 24 hour-urine calcium excretion decreased among hypercalciuric subjects after supplementation of calcium and vitamin D. However, an average 24 hour-urine calcium excretion among normocalciuric subjects did not change after supplementation of calcium and

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vitamin D. CTX, bone resorption marker was significantly decreased and spine BMD was significantly increased supplementation for 6 months.
Conclusion: Nutritional support including calcium supplementation should be required for the most postmenopausal women and should be required for the most persons who are interested in improving bone health.

25OH Vitamin D was measured with one of the BioSource (now DIAsource) 25OH Vitamin D3 RIA assay (KIP1961).

- KANG M.-I. (2008)

Short-term changes in bone and mineral metabolism following gastrectomy in gastric cancer patients.
Bone, 42(1):61-7

Changes in bone and mineral metabolism that occur after gastrectomy have long been recognized. Gastrectomy has been identified as a risk factor for decreased bone mass and the increased fracture incidence. Previous investigations concerning postgastrectomy bone disease have been observational studies. No prospective studies have been reported that quantify the amount of bone loss after gastrectomy within the same patients. This study investigated 46 patients undergoing gastrectomy for gastric adenocarcinoma and analyzed 36 patients (58.1+/-10.8 years, 24 men and 12 women) who had dual energy X-ray absorptiometry (DXA) performed before and 1 year after gastrectomy. Systemic adjuvant chemotherapy was administered to 14 patients. Blood was sampled from all patients to determine serum calcium, phosphorous, and bone turnover marker levels before gastrectomy and at 1, 3, 6 and 12 months after surgery and for serum parathyroid hormone (PTH) and 25-hydroxyvitamin D levels before and 12 months after surgery. The mean bone loss in the lumbar spine, total hip, femoral neck, and trochanter, which was calculated as the percentage change from the baseline to the level measured at 12 months, was 5.7% (P<0.01), 5.4% (P<0.01), 6.6% (P<0.01) and 8.7% (P<0.01), respectively. Bone loss was generally greater in the group receiving chemotherapy. The serum calcium and phosphorous levels were not changed significantly and remained within the normal range throughout the observation period. After gastrectomy, the level of ICTP increased and reached a peak at 1 and 3 months, and progressively declined to baseline by 12 months. The osteocalcin levels were not coupled to an increase before 6 months. The level of 25-hydroxyvitamin D at 12 months postgastrectomy was not significantly changed compared to the baseline, however, the PTH levels increased by a mean of 63.6% at 12 months compared to the baseline (P<0.01). Significant correlations were found between the percent change in the BMD at the lumbar spine and total hip and the percentage change for the PTH level from their baselines to 12 months. The changes in the BMD at total hip, femoral neck, and trochanter also correlated to the change in body weight at 12 months. The data obtained by this study provides evidence that profound bone loss occurs in the setting of a bone remodeling imbalance during the early postgastrectomy period and allows the speculation that the gastrectomy related bone loss may be partially due to an overproduction of PTH.

25OH Vitamin D was measured with one of the BioSource (now DIAsource) 25OH Vitamin D3 RIA assay (KIP1961).

- KANG M.-I. (2008)

Reappraisal of the Prevalence of Vitamin D Inadequacy in Korea: A Single Center's Experience.
Korean Journal of Bone Metabolism, 15(2):109-115

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연구목적: 최근의 연구에 따르면 대한민국의 평균 혈청 비타민 D 수치는 세계에서 하위권인 것으로 보인다. 이 런 결과는 혈청 비타민 D 측정 방법의 영향을 받은 것으로 보이며 본 연구에서는 국내 단일 병원에 내원한 여 성 환자들의 혈청 비타민 D 수치를 측정하고 기존의 견해에 대해 재고찰하였다. 방 법: 저자들은 2006 년 2 월부터 2008 년 2 월까지 성모 병원 내분비내과를 내원한 645 명의 여성을 대상으로 Biosource 방사선면역분석으로 측정한 혈청 25(OH)D 를 후향적으로 비교분석하였다. 결 과: 환자들의 25(OH)D 수치의 중앙값은 29.23 (interquartile range (IQR) 20.7~41.91) ng/mL 이었다. 335 (51.9%) 명의 환자들에서 25(OH)D 가 30 ng/mL 미만이었고 147 (22.8%) 명의 환자에서 20 ng/mL 미만이었다. 이변량 상관분 석에서 연령과 폐경 기간이 증가함에 따라 25(OH)D 농도는 감소하였다. 평균치 비교에서 25(OH)D 농도가 30 ng/mL 미만인 환자들이 30 ng/mL 이상인 환자들에 비해 연령이 높았고 폐경 후 기간이 길었으며 복용하는 비타민 제제의 농도가 더 높았다 (혈청 25(OH)D 측정 8 주 전부터 기준). 콜레칼시페롤 제제를 복용환 환자들이 에르고 칼시페롤 제제를 복용한 환자들에 비해 혈청 25(OH)D 농도의 증가폭이 컸다. 결 론: 본 연구에 의하면 국내 비타민 D 불충분 (inadequacy) 의 유병률이 기존에 알려진 것만큼 높지 않을 가 능성이 있다.

25OH Vitamin D was measured with one of the BioSource (now DIAsource) 25OH Vitamin D3 RIA assay (KIP1961).

- LARIJANI B. (2008)

Association between Vitamin D Deficiency and Unexplained Musculoskeletal Pain. Iranian J Publ. Health, A supplementary issue on Osteoporosis and Bone Turnover, 1:49-54

Background: Vitamin D is an essential element for establishing bone and muscle structures. Unexplained musculoskeletal (MSK) pain is a common problem in elderly. The aim of this study is investigation of association between vitamin D deficiency and unexplained MSK pain.
Methods: In order to quantify serum levels of vitamin D and other biochemical parameters, serum samples were taken from 1105 subjects aged from 17 to 79 years old, selected based on randomized clustered sampling from 50 blocks in Tehran Unexplained MSK pain was assessed based on the verbal rating scale.
Results: Prevalence of MSK pain was 4.4% in the group with normal serum vitamin D, 4.9% in the group of mild vitamin D deficiency, 7.4% in the group of moderate vitamin D deficiency and 11.3% in the group of severe vitamin D deficiency. There was also a relative risk for unexplained MSK pain of severe vitamin D deficiency of 1.26 (95%CI: 1.01–1.72). Odds Ratio was 4.65 (CI95%:1.25–17.3) in this women. We found quite a high prevalence of unexplained MSK pain in people participated in our study. We also found a Conclusion: Positive relationship between BMI and unexplained MSK pain.
Conclusion: vitamin D deficiency may be a major cause of unexplained MSK pain especially in older women.

25OH Vitamin D was measured with the BioSource (now DIAsource) 25OH Vitamin D3 RIA assay (KIP1961).

- DURSUN H. (2008)

Effects of Cirrhosis on Bone Mineral Density and Bone Metabolism EAJM, 40:18

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Objective: The present study was undertaken to examine the correlation between the severity of liver disease and the presence and severity of bone disease in patients with hepatic cirrhosis.
Materials and Methods: Between January 2005 and February 2006, 40 patients with cirrhosis and 22 healthy controls were enrolled in a cross-sectional study. All subjects underwent standard laboratory testing and bone densitometry studies of the lumbar spine and femoral neck using dual X-ray absorptiometry (DEXA).
Results: Cirrhotic patients had lower serum follicle-stimulating hormone (FSH) levels than controls. Male patients had lower serum free testosterone (fT) levels than male controls. 25-hydroxyvitamin D (25-OHD3) levels were significantly higher in the controls as compared to patients with cirrhosis. In the cirrhotic group, 25-OHD3 concentrations did not differ significantly between patients with Child B and C class cirrhosis. As compared to the control group, cirrhotic patients had significantly elevated levels of urinary deoxypyridinoline (DPD). The cirrhotic patients also had a significantly lower mean spinal (SD) bone mineral density (BMD) than the control group. BMD of the lumbar spine (LS) was noted to be significantly lower in the Child C group than in the Child B group. In the cirrhotic patients, there was a positive correlation between the BMD T score of the femoral neck (FN) and albumin levels whereas there was a negative correlation between BMD T scores of the FN and age, bilirubin and prothrombin time (PT).
Conclusion: Osteopenia and osteoporosis are highly prevalent in individuals with liver cirrhosis. Cirrhotic patients should undergo routine bone densitometry assessment and, if necessary, be treated for osteoporosis.

25OH Vitamin D was measured with the BioSource (now DIAsource) 25OH Vitamin D3 RIA assay (KIP1961).

- BOZKURT D. (2009)

Low Levels of 1.25-Dihydroxy Vitamin D is associated with All-cause Mortality in Prevalent Hemodialysis Patients.
Turkish Nephrology, Dialysis and Transplantation Journal, 19(1):11-16

It has been suggested that vitamin D contributes not only to bone mineral metabolism but also to important other physiological processes. Vitamin D levels have been associated with increased mortality in predialysis and incident HD patients, but no data is available on the association between vitamin D levels and survival in prevalent hemodialysis (HD) patients. Five hundred and forty five prevalent hemodialysis patients were recruited. Time averaged laboratory values throughout the two years and base line serum 25-OH vitamin D and 1.25-OH vitamin D levels were determined. All-cause mortality was prospectively evaluated after 2-year follow-up period. 25-OH vitamin D levels were significantly lower in females and in patients with diabetes. 1.25-OH2 vitamin D level was significantly lower in diabetics. After two years of follow-up period, in crude analysis low serum 25-OH and 1.25 OH2 vitamin D levels were associated with all-cause mortality. In adjusted Cox-regression analysis, 1.25-OH2 vitamin D level, but not 25-OH, was found as an independent predictor for all-cause mortality. Low 1.25-OH2 vitamin D level was also found as an independent predictor for all-cause mortality in non-diabetic study group even after inclusion of time averaged vitamin D therapy dosage.

25OH Vitamin D and $1,25(OH)_2$ Vitamin D were measured with respectively the BioSource Europe (now DIAsource) 25OH Vitamin D3 RIA assay (KIP1961) and $1,25(OH)_2$ Vitamin D RIA assay (KIP1929).

- KIM S.H. (2009)

The level of vitamin D in the serum correlates with fatty degeneration of the muscles of the rotator cuff.

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J Bone Joint Surg., 91-B:1587-93

This study examined the role of vitamin D as a factor accounting for fatty degeneration and muscle function in the rotator cuff. There were 366 patients with disorders of the shoulder. A total of 228 patients had a full-thickness tear (group 1) and 138 patients had no tear (group 2). All underwent magnetic resonance arthrography and an isokinetic muscle performance test. The serum concentrations of vitamin D (25(OH)D3) were measured. In general, a lower serum level of vitamin D was related to higher fatty degeneration in the muscles of the cuff. Spearman's correlation coefficients were 0.173 (p = 0.001), -0.181 (p = 0.001), and -0.117 (p = 0.026) for supraspinatus, infraspinatus and subscapularis, respectively. In group 1, multivariate linear regression analysis revealed that the serum level of vitamin D was an independent variable for fatty degeneration of the supraspinatus and infraspinatus. The serum vitamin D level has a significant negative correlation with the fatty degeneration of the cuff muscle and a positive correlation with isokinetic muscle torque.

25OH Vitamin D was measured with the BioSource Europe (now DIAsource) 25OH Vitamin D3 RIA assay (KIP1961).

- JOH H.-K. (2009)

Biochemical Markers and Health Behavior Related with Bone Mineral Density in Adult Men.
Korean J Fam Med, 30:359-368

Background: More than half of the causes of male osteoporosis is due to secondary osteoporosis. Therefore, it is important to detect and modify its related factors. The aim of this study was to find related lifestyle factors and biochemical markers with low bone mineral density (BMD) in Korean men.
Methods: A cross-sectional analysis was performed in men aged 40-69 years who visited a hospital for health checkup from January to March 2007. BMD was measured at proximal femur and lumbar spine by dual energy x-ray absorptiometry. Lifestyle factors were estimated by a self-administered questionnaire and fasting glucose, uric acid, gamma glutamyltransferase, alkaline phosphatase, creatinine, free testosterone, 25-OH vitamin D, urine deoxypyridinoline, osteocalcin were measured. Multivariate logistic regression was used to fi nd the association to the lowest tertile of BMD.
Results: A total of 152 subjects were included. After multivariate analysis adjusted with age, BMI, smoking, alcohol and exercise, different factors were correlated with low bone density in each site of femoral neck and lumbar spine. Factors correlated at both sites were BMI and exercise; lower BMI and doing no exercise increased risks of low bone density. Increasing age and alcohol intake ≥ 14 drinks/week were associated with lower BMD at femoral neck. The factors associated with lower lumbar spine BMD only were lower level of uric acid and higher level of urine deoxypyridinoline.
Conclusion: Different factors were associated with low bone density at femoral neck and lumbar spine in men. BMI and exercise were related in both sites; age, alcohol intake, uric acid and deoxypyridinoline were related on either site.

25OH Vitamin D was measured with the BioSource Europe (now DIAsource) 25OH Vitamin D3 RIA assay (KIP1961).

- PARK J. (2009)

Vitamin D Levels and Their Relationship with Cardiac Biomarkers in Chronic Hemodialysis Patients.
J Korean Med. Sci, 24(Suppl. 1):S109-14

Vitamin D insufficiency may be associated with cardiovascular (CV) mortality in HD patients. To test this hypothesis, we cross-sectionally measured 25-hydroxyvitamin D (25D), 1,25-dihydroxyvitamin D

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(1,25D), cardiac troponin T (cTnT), and N-terminal pro-B-type natriuretic peptide (NT-pro-BNP) in chronic HD patients. Sixty-five patients (M:F=31:34, age 52.2±13.2 yr, DM 41.5%) were selected. Along with the expected low levels of 1,25D, 59 (90.8%) patients had 25D insufficiency (<30 ng/mL) among whom 15 (23.1%) were 25D deficient (<10 ng/mL). The 25D levels showed a negative correlation with cTnT levels (Spearman's ρ=-0.44, p<0.01) but not with NT-pro-BNP levels (Spearman's ρ=-0.17, p=0.17). The 1,25D levels, however, did not show any relationship with either cTnT or NT-pro-BNP. In multivariate analysis, being male and having low levels of 25D were independent risk factors associated with cTnT elevation (β=0.44, p<0.01 and β=-0.48, p<0.01, respectively). In conclusion, not only 1,25D but also 25D are commonly decreased in HD patients. Lower 25D levels appear to be associated with cTnT elevation, predicting worse CV outcome, and are possible to involve cardiac hypertrophy or coronary artery disease.

25OH Vitamin D was measured with the BioSource Europe (now DIAsource) 25OH Vitamin D3 RIA assay (KIP1961).

- MADDAH M. (2009)

Intake of calcium/vitamin D supplement in Iranian postmenopausal women.
Arch Osteoporos, 4:95–96

This study is part of a survey conducted to examine prevalence of osteoporosis among elderly women in Guilan, northern Iran. A total of 504 women from urban areas and 291 women from rural areas were selected. Diagnosis of osteoporosis was carried out using quantitative ultrasound technique and positive cases were confirmed by dual X-ray absorptiometry [4]. Serum 25(OH) D3 was measured using a commercial kit (BioSource 25OH-Vit.D3-CT Kit).

25OH Vitamin D was measured with the BioSource Europe (now DIAsource) 25OH Vitamin D3 RIA assay (KIP1961).

- BONAKDARAN S. (2009)

Correlation between serum 25 hydroxy vitamin D3 and laboratory risk markers of cardiovascular diseases in type 2 diabetic patients.
Saudi Med. J, 30(4):509-514

Objectives: To determine the association between vitamin D deficiency and cardiovascular risk markers among diabetic patients.
Methods: This was a cross-sectional study conducted in Ghaem Hospital, Mashhad, Iran, from December 2007 to March 2008 in 119 type 2 diabetic patients. Coronary, cerebrovascular, and peripheral vascular diseases were confirmed. Blood biochemical parameters including laboratory risk markers of cardiovascular disease were determined. Serum 25 hydroxy (OH) D was measured during winter. The correlation between vitamin D deficiency and cardiovascular prevalence, and also laboratory variables was determined.
Results: The mean age of patients was 55.3 ± 11.2 years. The mean 25(OH) D concentration was 32.4 ± 21.6ng/ml. The prevalence of hypovitaminous D was 26.1% among the diabetic patients. The difference with the control group was not significant (p=0.12). Overall, 36 (30.3%) patients were positive for coronary vascular disease (CVD). The correlation between hypovitaminous D and CVD was not significant (p=0.11). Patients with vitamin D deficiency had significant differences in body mass index (p=0.003), metabolic syndrome (p=0.05), high sensitive C-reactive protein (p=0.009), microalbuminuria (p=0.04), and glomerular filtration rate (p=0.02), compared to patients with sufficient vitamin D. The fasting blood sugar, glycosylated hemoglobin, lipid profiles, homocysteine, uric acid, and insulin resistance were not related to vitamin D deficiency.
Conclusion: There is an association between hypovitaminous D and inflammatory markers that contributed to CVD, so vitamin D may be important in maintaining cardiovascular health.

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25OH Vitamin D was measured with one of the BioSource Europe (now DIAsource) 25OH Vitamin D RIA assay (KIP1961 or KIP1971).

- CORTADELLAS O. (2009)

Calcium and Phosphorus Homeostasis in Dogs with Spontaneous Chronic Kidney Disease at Different Stages of Severity.
J Vet. Intern. Med., 24:73–79

Background: Studies in dogs with experimental chronic kidney disease (CKD) have demonstrated that abnormalities of calcium-phosphorus (Ca-P) homeostasis occur frequently and have a negative effect on kidney function and survival. However, the prevalence of these alterations in dogs with naturally occurring CKD at different stages of severity has not yet been investigated.
Hypothesis: Abnormalities of Ca-P metabolism occur early in the course of CKD with an increased prevalence in more severe stages.
Animals: Fifty-four dogs with CKD and 22 healthy dogs.
Methods: Blood and urine samples were obtained for a CBC, biochemistry, determination of parathyroid hormone (PTH), calcitriol, and ionized calcium concentrations and urinalysis. Based on urine protein/creatinine ratio and serum creatinine concentration, dogs were grouped according to the IRIS classification for CKD.
Results: Hyperparathyroidism (HPTH) (PTH 48 pg/mL) was diagnosed in 41 (75.9%) dogs with CKD. Its prevalence increased from 36.4% (stage 1) to 100% (stage 4). Hyperphosphatemia (P 4 5.5 mg/dL) was present in 37 (68.5%) dogs; increasing in prevalence from 18% (stage 1) to 100% (stage 4). Receiver-operating characteristic curve analysis showed that serum phosphorus concentration in the 4.5–5.5 mg/dL range correctly identified the presence of HPTH in most dogs. Calcitriol concentration progressively decreased in dogs with CKD and differences became statistically significant by stage 3.
Conclusion and Clinical Relevance: HPTH and hyperphosphatemia occur frequently in dogs with naturally occurring CKD, even at early stages of CKD in some dogs. These findings highlight the importance of monitoring these parameters early in the course of CKD.

$1,25(OH)_2$ Vitamin D was measured with the BioSource Europe (now DIAsource) $1,25(OH)_2$ Vitamin D RIA assay (KIP1929).

- YAVUZ B. (2010)

STATIN-D Study: Comparison of the Influences of Rosuvastatin and Fluvastatin Treatment on the Levels of 25 Hydroxyvitamin D.
Cardiovascular Therapeutics, 00:1–7

Several studies have shown that low 25-hydroxyvitamin D levels are associated with higher risk of cardiovascular disease and an increase in 25-hydroxyvitamin D levels protects against cardiovascular disease. In this study, we aimed to compare the effects of rosuvastatin and fluvastatin on vitamin D metabolism. The study population consisted of 134 hyperlipidemic patients who had not previously been treated with lipid lowering medications. Patients were randomized in a 1:1 ratio to rosuvastatin 10 mg or fluvastatin 80 mg XL during the study. Lipid parameters, 25 hydroxyvitamin-D, and bone alkaline phosphatase (BALP) were obtained at baseline and after 8 weeks of rosuvastatin and fluvastatin treatment. Sixty-nine patients were administered rosuvastatin, and 65 patients fluvastatin. Total Cholesterol and LDL cholesterol decreased after 8 weeks of both rosuvastatin and fluvastatin treatments. Rosuvastatin was significantly more effective than fluvastatin on lowering total ($P < 0.001$) and LDL cholesterol ($P < 0.001$). There was a significant increase in 25-hydroxyvitamin D with rosuvastatin treatment ($P < 0.001$), whereas no significant change in 25-hydroxyvitamin D was observed with fluvastatin treatment. Mean BALP fell from 18.5 to 9.6 u/I ($P < 0.001$) with rosuvastatin

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and from 17.0 to 12.8 with fluvastatin (P = 0.004). There was no significant difference in BALP levels between rosuvastatin and fluvastatin treatment (P = 0.368). The present study demonstrated that 25-hydroxyvitamin D levels increased with rosuvastatin treatment; whereas fluvastatin treatment had no effect on 25-hydroxyvitamin D. This disparity could be related to the potency or the bioavailability of these two statins. Further studies are needed to clarify the relationship between statins and the vitamin D physiology.

25OH Vitamin D was measured with the BioSource Europe (now DIAsource) 25OH Vitamin D3 RIA assay (KIP1961).

- KIM M.-J. (2010)

Nutritional Status of Vitamin D and the Effect of Vitamin D Supplementation in Korean Breast-fed Infants.
J Korean Med. Sci, 25:83-9

We investigated the vitamin D status and the effect of vitamin D supplementation in Korean breast-fed infants. The healthy term newborns were divided into 3 groups; A, formula-fed; B, breast-fed only; S, breast-fed with vitamin D supplementation. We measured serum concentrations of vitamin D (25OHD3), calcium (Ca), phosphorus (P), alkaline phosphatase (AP), intact parathyroid hormone (iPTH) and bone mineral density (BMD) at 6 and 12 months of age. Using questionnaires, average duration of sun-light exposure and dietary intake of vitamin D, Ca and P were obtained. At 6 and 12 months of age, 25OHD3 was significantly higher in group S than in group B (P<0.001). iPTH was significantly lower in group S than in group B at 6 months (P=0.001), but did not differ at 12 months. Regardless of vitamin D supplementation, BMD was lower in group B and S than in group A (P<0.05). Total intake of vitamin D differed among 3 groups (P<0.001, A>S>B), but total intake of Ca and P were higher in group A than in group B and S (P<0.001). In conclusion, breast-fed infants show lower vitamin D status and bone mineralization than formula-fed infants. Vitamin D supplementation (200 IU/day) in breast-fed infants increases serum 25-OH vitamin D3, but not bone mineral density.

25OH Vitamin D was measured with the BioSource Europe (now DIAsource) 25OH Vitamin D3 RIA assay (KIP1961).

- CHO C.Y. (2010)

The Relationship between Vitamin D Levels and Chronic Diseases.
Korean J Clin Geri, 11(2):154-169

Background: Vitamin D deficiency is prevalent worldwide, not only in patients with osteoporosis but also in normal adults. Because the situation is especially severe in Korea. So, we take a look at the degree of vitamin D deficiency in Korea and the relationship between chronic diseases which are common in primary care and vitamin D level.
Methods: 200 patients above the age of 20, who were admitted to the Department of Family Medicine at Soonchunhyang University from June of 2009 to May of 2010 were chosen. Questionnaires regarding the patients' drug history and afflicted disease and the average serum 25-hydroxyvitamin D, 1,25-dihydroxyvitamin D levels were obtained and we looked into their relationships to the diagnosed chronic disease or possessed chronic disease such as like diabetes, hypertension, osteoporosis, hyperlipidemia.
Results: In our study a serum 25(OH)D level lower than 80 nmol/dL (32 ng/mL) was considered vit D deficient. 127 patients (63.5%) were deficient in vit D and 126 patients (73%) were beyond adequacy. The serum 25(OH)D showed a significant positive relationship with total cholesterol (P=0.01), triglyceride (P=0.049), High density lipoprotein-cholesterol (P=0.001), and Low density lipoprotein-cholesterol (P=0.007). The serum 1,25(OH)2D3 showed a significant negative relationship with Triglyceride (0.018). The serum 25(OH)D level was not shown any significant effect by Fasting plasma

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glucose, HbA1c, Total cholesterol, Triglyceride, High density lipoprotein, Low density lipoprotein. The serum 25(OH)D showed no significant relationship with the presence of existing diseases as diabetes, hypertension, hyperlipidemia, osteoporosis or newly diagnosed as same above at admitted. also, the serum 1,25 (OH)2D3 showed a significant negative relationship with the presence of existing diseases as diabetes, hypertension, hyperlipidemia, osteoporosis or newly diagnosed as same above at admitted. Preexisting treatment history or newly diagnosed at admission of diabetes (P=0.003) and hypertension (P=0.009) showed a significant inversely proportional correlation to the serum 1,25 (OH)2D3 level and of hyperlipidemia showed a significant directly proportional relationship to the serum 1,25 (OH)2D3 level (P=0.008).
Conclusion: About a two-thirds of those surveyed is found to have vitamin D deficiency. Vitamin D, in addition to its role in bone metabolism, seems to have an effect on the genesis of hypertension and diabetes. So, it is considered that a further prospective study on the clinical usefulness of vitamin D will be needed for chronic diseases increases due to the increase of the elderly population.

25OH Vitamin D was measured with the BioSource Europe (now DIAsource) 25OH Vitamin D3 RIA assay (KIP1961).

- MEI W. (2010)

Overexpression of parathyroid pituitary-specific transcription factor (Pit)-1 in hyperphosphatemia-induced hyperparathyroidism of chronic renal failure rats. Chin. Med. J, 123(12):1566-1570

Background: Hyperphosphatemia in renal failure has been identified as a major role in the pathogenesis of hyperparathyroidism that is independent of changes in serum calcium and 1,25(OH)2D3. The aim of this study was to evaluate the expression of parathyroid Pit-1 in hyperphosphatemia-induced secondary hyperparathyroidism (SHPT) of chronic renal failure (CRF) rats.
Methods: Wistar rats with CRF induced by 5/6 nephrectomy were ramdomly fed with diet containing 1.2% inorganic phosphate (Pi, high phosphate (HP) group, n=9) or 0.2% Pi (low phosphate (LP) group, n=9) for 10 weeks starting from the fourth week after the surgery. Another 7 nephrectomy rats with HP diet were intraperitoneally injected with phosphonoformic acid (PFA, the specific inhibitor of Pit-1, HP+PFA group) 0.15 g/kg every other day for 10 weeks starting from HP diet. Another 6 HP rats injected with the same amount of normal saline as the control of the HP+PFA group (HP+saline group). At the same time, 9 rats with sham surgery received HP diet as the controls. At the 4th week and 14th week, blood was taken for measurement of serum creatinine (SCr), serum calcium (SCa), serum phosphorus (SPi), 1,25(OH)2D3 and intact parathyroid hormone (iPTH). At the 14th week, two parathyroid glands (PTGs) of each rat were removed by microsurgery, one gland for immunohistochemistry analysis of proliferating cell nuclear antigen (PCNA), the other one for detection of Pit-1 by Western blotting, and for the measurement of Pit-1 mRNA and PTH mRNA by real-time quantitative polymerase chain reaction.
Results: In nephrectomy rats, high dierary phosphate induced a marked increase in serum phosphate, iPTH, PTH mRNA and PCNA parathyroid cells, accompanying Pit-1 and its mRNA in parathyroid gland increased significantly. However, serum Ca and 1,25(OH)2D3 remained unchanged. PFA decreased Pit-1 and its mRNA levels to reduce intact PTH, PTH mRNA and PCNA-positive parathyroid cells.
Conclusions: Expression of parathyroid Pit-1 in hyperphosphatemia-induced SHPT of CRF rats was upregulated. Pit-1 may mediate the stimulation to parathyroid gland by hyperphosphatemia.

$1,25(OH)_2$ Vitamin D was measured with the BioSource (now DIAsource) $1,25(OH)_2$ Vitamin D RIA assay (KIP1921, now KIP1929).

- KARADAĞ A.S. (2011)

The role of anemia and vitamin D levels in acute and chronic telogen effluvium.

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Turk. J Med. Sci, 41(5):827-833

Aim: Telogen effluvium (TE) is an abnormality of hair cycling. Vitamin D promotes hair follicle differentiation. The importance of vitamin D in hair growth is evident in patients with hereditary vitamin D receptor deficiency. The role of vitamin D in the pathogenesis of TE has not been investigated before. We investigated the role of vitamin D, ferritin, and zinc in the pathogenesis of TE.
Materials and methods: We measured serum hemoglobin, ferritin, zinc, calcium, phosphate, parathormone, magnesium, 25 and 1,25-hydroxyvitamin D3, and bone alkaline phosphatase and thyroid stimulating hormone levels in 63 female patients and 50 control subjects. Twenty-nine of the TE patients were classified in the acute TE group and 34 were classified in the chronic TE groups.
Results: Ferritin (acute TE; 17.0 ± 12.8, chronic TE; 19.6 ± 15.2, control; 35.5 ± 31.8, P < 0.001) and hemoglobin (acute TE; 12.7 ± 1.7, chronic TE; 13.3 ± 1.0, control; 14.2 ± 1.2, P < 0.0001) levels were significantly lower in the TE group than in the control group. However, 25-hydroxyvitamin D3 levels were significantly higher in the TE group than in the control group (acute TE; 18.5 ± 9.2, chronic TE; 24.4 ± 11.2, control; 15.6 ± 15.8, P < 0.01). Vitamin D levels increased gradually from control groups to acute and chronic TE groups. However, active D vitamin levels (1,25-hydroxyvitamin D3) were similar.
Conclusion: Iron deficiency anemia seems to be the main triggering factor for the development of TE and the increase in serum 25-hydroxyvitamin D3 levels may be related to increased exposure to UV light due to TE.

25OH Vitamin D and 1,25$(OH)_2$ Vitamin D were measured with respectively the BioSource Europe (now DIAsource) 25OH Vitamin D3 RIA assay (KIP1961) and 1,25$(OH)_2$ Vitamin D RIA assay (KIP1921, now KIP1929).

- KHADER Y.S. (2011)

Relationship between 25-hydroxyvitamin D and metabolic syndrome among Jordanian adults.
Nutr. Res. Pract., 5(2):132-139

Evidence of the association between 25-hydroxyvitamin D (25(OH)D) and metabolic syndrome (MeS) remains uncertain and incongruent. This study aimed to determine the association between 25(OH)D and MeS among Jordanian adults. A complex multistage sampling technique was used to select a national population-based household sample. The present report deals exclusively with adults aged >18 years who had complete information on all components of MeS (n = 3,234). A structured questionnaire was used to collect all relevant information. Anthropometric, clinical, and laboratory measurements were obtained. MeS was defined according to the International Diabetes Federation (IDF) definition. Of the total, 42.0% had MeS and 31.7% had 25(OH)D < 30 ng/ml. In a stratified analysis, the prevalence of MeS did not differ significantly between subjects with low and normal 25(OH)D levels for men and women in all age groups. In the multivariate analysis, the odds of MeS were not significantly different between subjects with low and normal 25(OH)D levels (OR = 0.85, 95% CI: 0.70, 1.05, P-value = 0.133). The association between 25(OH)D and MeS remained non-significant when 25(OH)D was analyzed as a continuous variable (OR = 1.004, 95% CI; 1.000, 1.008, P = 0.057) and when analyzed based on quartiles. None of the individual components of MeS were significantly associated with 25(OH)D level. This study does not provide evidence to support the association between 25(OH)D level and MeS or its individual components. Prospective studies are necessary to better determine the roles of 25(OH)D levels in the etiology of MeS.

25OH Vitamin D was measured with the BioSource Europe (now DIAsource) 25OH Vitamin D3 RIA assay (KIP1961).

- PARK S.Y. (2011)

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Vitamin D Inadequacy in Patients with Osteoporotic Hip Fractures.
Korean J Bone Metab, 18(1):9-14

OBJECTIVE: To investigate the prevalence of vitamin D inadequacy in an elderly patients with hip fracture.
METHODS: A prospective study was carried out for 2 years (January 2008 - December 2009). Patient records were searched for hip fracture admission and cross matched with serum vitamin D levels and bone densitometry carried out within 3 days of the hip fracture admission.
RESULTS: There were data for 115 hip fracture patient, 69% of the patients were women (n = 79). The mean age at the time of fracture was 76.1 years. The mean of bone densitometry was -2.8 +/- 0.8. About 40% of the patients had a bone mineral density (BMD) below -3.0. The mean vitamin D (25-OH) level was 20.9 +/- 10 ng/mL. Over 80% of patients had a vitamin D level below 30 ng/mL. Especially, patients (n = 17) admitted from assisted nursing home had less a vitamin D level (16.3 ng/mL) than patients admitted from home (22.9 ng/mL). There were no significant differences by age or sex however, there was seasonal differences in vitamin D.
CONCLUSION: This study reveals universal vitamin D inadequacy in hip fracture patients.

25OH Vitamin D was measured with the BioSource Europe (now DIAsource) 25OH Vitamin D3 RIA assay (KIP1961).

- MIRSHAFIEY A. (2011)

Randomized controlled trial using vitamins E and D supplementation in atopic dermatitis.
Journal of Dermatological Treatment, 22:144–150

Background: Atopic dermatitis is a chronically relapsing, highly pruritic and inflammatory skin disease. This study was done to assess the effects of vitamins D and E supplementation on the clinical manifestation of atopic dermatitis.
Methods: Forty-five atopic dermatitis patients were included in a randomized, double-blind, placebo-controlled trial. They were randomly divided into four groups and treated for 60 days: group P (n = 11), vitamins D and E placebos; group D (n = 12), 1600 IU vitamin D3 plus vitamin E placebo; group E (n = 11), 600 IU synthetic all-rac-a-tocopherol plus vitamin D placebo; and group DE (n = 11), 1600 IU vitamin D3 plus 600 IU synthetic all-rac-a-tocopherol. Serum 25(OH) vitamin D and plasma a-tocopherol were determined before and after the trial. The clinical improvement was evaluated with SCORing Atopic Dermatitis (SCORAD). Data were analyzed by analysis of variance (ANOVA) and Kruskal-Wallis tests.
Results: SCORAD was reduced after 60 days in groups D, E and DE by 34.8%, 35.7% and 64.3%, respectively (p = 0.004). Objective SCORAD also showed significant improvement. There was a positive correlation between SCORAD and intensity, objective, subjective and extent (p < 0.001). We found a significant negative association between plasma a-tocopherol and SCORAD, intensity, objective and extent (p = 0.02).
Conclusion: This study supports the contributing and beneficial effects of vitamins D and E in the treatment of atopic dermatitis.

25OH Vitamin D was measured with the BioSource Europe (now DIAsource) 25OH Vitamin D3 RIA assay (KIP1961).

- LI B.-Y. (2011)

Enhanced Radiosensitivity in 1,25-dihydroxyvitamin D3 Deficient Mice.
J. Radiat. Res., 52:215–219

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To investigate whether impaired osteogenesis resulting from vitamin D deficiency can influence hematopoiesis recovery after radiation, the 25-hydroxyvitamin D-1α-hydroxylase (1α-hydroxylase) gene knockout (KO) mice and wild type (WT) mice were subjected to different doses of gamma ray. The survival rates, peripheral blood cell counts and bone marrow cellularity were studied after irradiation (IR). The survival rates of the KO mice were significantly lower than that of WT mice after 6 or 8 Gy dose of radiation. The recovery of white blood cells in KO mice was significantly delayed compared with that in WT mice after radiation. The red blood cell number in WT mice was observed to increase more than that in KO mice at days 14 and 28 after radiation. The nadir platelet count in KO mice was nearly half of that in WT mice. Dramatically higher bone marrow cell numbers were found in WT mice compared with KO mice. Our findings demonstrate the enhanced radiosensitivity in 1,25-dihydroxyvitamin D3 (1,25-(OH)2D3) deficient mice.

$1,25(OH)_2$ Vitamin D was measured with the BioSource (now DIAsource) $1,25(OH)_2$ Vitamin D RIA assay (KIP1921, now KIP1929).

- JAHANSHAHIFAR L. (2011)

Vitamin D deficiency and its association with disease activity in new cases of systemic lupus erythematosus.
Lupus, 20:1155-1160

Evidence has shown a relationship between vitamin D deficiency and systemic lupus erythematosus (SLE). We evaluated the frequency of vitamin D deficiency and its association with disease activity in new cases of SLE. Women with newly diagnosed SLE, based on the American College of Rheumatology (ACR) criteria, were enrolled consecutively. Those receiving vitamin D supplements and postmenopausal women were not included. Disease activity was measured by the BILAG index (2004) and serum concentration of 25-hydroxyvitamin D (25[OH]D) was measured by radioimmunoassay method. Forty SLE patients with mean age of 25.3±4.2 years were studied. Severe, moderate, and mild vitamin D deficiency, corresponding to serum 25[OH]D concentrations of <12.5, 12.5–24.9, and 25–39.9 nmol/l, were found in 12.5%, 62.5%, and 17.5% of the patients, respectively. Serum 25[OH]D concentration was inversely correlated with the British Isles Lupus Assessment Group (BILAG) index score (r=-0.486, p=0.001). Those with a more severe vitamin D deficiency had also higher concentrations of liver enzymes (p<0.05), lower serum albumin and hemoglobin concentrations (p<0.05), and higher titers of antibodies to double-stranded DNA (ds-DNA) (p<0.001). This study showed that most of the SLE patients in our society have vitamin D deficiency at the time of diagnosis that is associated with a higher disease activity. Routine screening for vitamin D deficiency and its prompt treatment in patients with newly diagnosed SLE is recommended.

25OH Vitamin D was measured with one of the DIAsource 25OH Vitamin D RIA assay (KIP1961 or KIP1971).

- DABAK M. (2011)

Vitamin D Status in Cattle with Malignant Catarrhal Fever.
J. Vet. Med. Sci., 74(1):125–128

The aim of the present study was to determine the vitamin D status in cattle with malignant catarrhal fever (MCF). Twelve cattle diagnosed as MCF and 6 healthy cattle (controls) were used in the study. Serum 1,25-dihydroxyvitamin D3 (1,25-D), 25-hydroxyvitamin D3 (25-D), calcium, phosphorus and parathyroid hormone (PTH) levels were determined as 96.83 pg/ml, 30.0 ng/ml, 2.19 mmol/l, 1.57 mmol/l and 15.21 pg/ml in MCF group and 42.33 pg/ml, 37.0 ng/ml, 2.43 mmol/l, 1.96 mmol/l and 36.08 pg/ml in controls, respectively. Although serum 1,25-D level in the MCF group was increased (P<0.01), serum calcium (P<0.01) and PTH (P<0.05) levels were decreased compared to the controls. The results suggest that there might be an interaction between vitamin D status and MCF.

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$1,25(OH)_2$ Vitamin D was measured with the DIAsource $1,25(OH)_2$ Vitamin D RIA assay (KIP1929).

- FELSENBERG D. (2011)

Additive impact of alfacalcidol on bone mineral density and bone strength in alendronate treated postmenopausal women with reduced bone mass.
J Musculoskelet. Neuronal Interact., 11(1):34-45

Objectives: Assessment of additive impact of alfacalcidol 1 µg daily (Alfa) on bone mineral density (BMD) and on bone strength in postmenopausal women treated with alendronate 70 mg weekly + 500 mg calcium daily.
Subjects and methods: In a randomized, double-blind, placebo controlled study, 279 postmenopausal women with osteoporosis or osteopenia participated (intention to treat analysis [ITT]; aged 73.6±4.7 years) and were treated with 70 mg alendronate (ALN) weekly and 500 mg calcium daily for 36 months. In addition, these patients received either 1 µg alfacalcidol (Alfa) or placebo (PLC) daily. BMD was measured with DualEnergy-X-ray-Absorptiometry (DXA) at the lumbar spine and proximal femur and at forearm and tibia with peripheral quantitative computed tomography (pQCT) at regular intervals for 36 months.
Results: DXA-BMD of lumbar spine (L1-4) increased after 36 months, by 6.65% (p<0.0001) in the Alfa/ALN group versus 4.17% (p<0.0001) in the PLC/ALN group. Group difference was significant after 3 years (p=0.026). At the end of the study, significant differences were found in favor of the Alfa/ALN group in trabecular density (tibia) (p=0.002), cortical density (midshaft tibia) (p=0.043), and bone strength (p=0.001). The remaining parameters showed no differences between the treatment arms, apart cortical bone density at midshaft radius.
Conclusions: Alfacalcidol significantly increases the efficacy of alendronate treatment in osteopenic/osteoporotic postmenopausal women on spinal DXA-BMD, cortical and trabecular BMD of the tibia and also bending stiffness of the tibia.

$1,25(OH)_2$ Vitamin D was measured with the DIAsource $1,25(OH)_2$ Vitamin D RIA assay (KIP1929).

- EL KHASMI M. (2011)

Circulating levels of 25-hydroxyvitamin D and testosterone during the rutting and non-rutting periods in Moroccan dromedary camels (Camelus dromedarius).
Emir. J. Food Agric., 23(4):368-374

The camel is largely known to be a seasonal breeder, thus, in the male camel, the breeding activity maximizes during the rutting period (winter and spring seasons) but ceases completely during the non-rutting period (summer and autumn). Plasma vitamin D3 concentrations showed significant seasonal variations; the purpose of this study was to investigate a possible role of vitamin D in the sexual activity in Moroccan dromedary camels by evaluating the variation in plasma vitamin D, calcium, and phosphorus concentrations in relation to those of testosterone during these two periods. Blood samples were collected from 14 adult male camels aged 5-8 years, slaughtered during March (n=7) and September (n=7) at the Tit-Mellil Municipality slaughterhouse. All animals were clinically healthy and blood samples were taken at 06 h AM into heparinized tubes. In the work reported here, our results showed that plasma levels of 25-hydroxyvitamin D were significantly higher and those of testosterone were significantly lower in the non-rutting animals when compared to the rutting ones (p<0.005). While, the plasma levels of calcium and inorganic phosphorus showed no seasonal variation. Based on the values obtained in this investigation, vitamin D does not appear to contribute directly or indirectly to camel steroidogenesis. Further studies, from the one hand of an eventual

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relationship between T and other parameters such as thyroid hormones and corticoids, and from the another one of testing the vitamin D action on rutting behavior are needed in camels.

25OH Vitamin D was measured with one of the DIAsource 25OH Vitamin D RIA assay (KIP1961 or KIP1971).

- LESIAK A. (2011)

The influence of phototherapy with narrow band UVB on 25-hydroxycholecalciferol serum concentration in psoriasis vulgaris patients.
Post Dermatol. Alergol., 2:97–102

Introduction: Narrow band UVB (311-313 nm) is commonly used in the treatment of many skin diseases, including psoriasis vulgaris. Under skin exposure to UVB synthesis of vitamin D occurs.
Aim: The aim of the study was to assess the serum concentration of vitamin D in psoriasis vulgaris as well as the changes in 25-hydroxycholecalciferol (25(OH)D) and parathormone (PTH) serum level under a series of UVB exposures. Additionally, we checked the correlation between the final vitamin D concentration and cumulative NB-UVB dose.
Material and methods: The study group included 47 patients with psoriasis vulgaris in the age range 20-65 years old. The patients were treated with 20 NB-UVB exposures. In each patient, 25(OH)D (RIA – radioimmunoassay) and PTH (immunochemiluminescence assay) serum concentration was checked 3 times: before therapy, and after 10 and 20 exposures.
Results: Baseline vitamin D concentration was 26.5 ng/ml. After the first 10 NB-UVB exposures vitamin D serum concentration statistically increased to the value of 38 ng/ml ($p < 0.001$), and after the next 10 irradiations 25(OH)D level increased (43 ng/ml), although it did not significantly differ compared to the second measurement ($p > 0.05$). A PTH serum concentration did not statistically change during the whole therapy. A positive correlation between the cumulative NB-UVB dose and the final 25(OH)D serum concentration was observed ($p < 0.05$).
Conclusions: Deficiency of vitamin D serum level is observed in psoriatic patients. NB-UVB significantly increases 25(OH)D synthesis dependently on cumulative dose, with no effect on PTH serum level. The lower increase in the vitamin D level in the course of phototherapy testifies to the photo adaptation phenomenon.

25OH Vitamin D was measured with one of the DIAsource 25OH Vitamin D RIA assay (KIP1961 or KIP1971).

- MAJAK P. (2011)

Vitamin D supplementation in children may prevent asthma exacerbation triggered by acute respiratory infection.
J Allergy Clin Immunol, 127(5):1294-6

25OH Vitamin D was measured with the DIAsource 25OH Vitamin D3 RIA assay (KIP1961).

- KOLANKO M. (2012)

Calcidiol level in patients with psoriasis treated with NB-UVB therapy.
Postępy Nauk Medycznych 10:s.787-793

Introduction. UVB 311nm phototherapy (NB-UVB) appears to influence the psoriasis significant factor's genes expression by epidermal syntesis of vitamin D.

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Aim. The aim of this research was to examine whether NB-UVB was able to induce 25(OH)D synthesis in relationship to its initial level and BMI, age, sex, nutrition and behavioral habits.
Material and methods. Serum 25(OH) D level was measured using RIA-method in 36 patients in T0 before the first dose of radiation, in T1-T3 during the treatment and in T4 and T5 accordingly in 1st and 5th week after the end of phototherapy. The parameters in controls (28 healthy adults) were measured in T0 and T4. Assessment included also: BMI, PASI, skin phototype, questionnaire (sun exposure, nutrition habits).
Results. Calcidiol level in T0 was higher in patients 33.21 nmg/ml vs. 25.17 ng/ml in controls ($p < 0.05$). The tendency to lower calcidiol levels among older, women and in patients with a lower PASI index value wasn't significant ($p > 0.05$). There was a statistically significant difference in the increase of calcidiol level in patients between T0 and T4 – higher in the group of level < 25 ng/ml. There was an increase of calcidiol level in patients in T4 – 50.16 ng/ml ($p < 0.05$) and a decrease in controls – 21.37 ng/ml. In T5 calcidiol level in patients was 51.18 ng/ml. 11-45% participants reported consumption of different dairy products. The consumption of fish was declared as at least once a month.
Conclusions. The initial level of 25(OH)D has an impact on its growth by NB-UVB. The dose of UVB 311 nm received during the irradiation masked seasonal variability of the calcidiol level. There was no effect of BMI or PASI index values, age or gender on the calcidiol level. Nutrition and behavioral habits have an impact on the calcidiol level.

25OH Vitamin D was measured with the DIAsource 25OH Vitamin D Total RIA assay (KIP1971).

- SCHAALAN M.F. (2012)

Vitamin D deficiency: Correlation to interleukin-17, interleukin-23 and PIIINP in hepatitis C virus genotype 4.
World J Gastroenterol., 18(28):3738-3744

AIM: To assess vitamin D (Vit D) abnormalities in hepatitis C infected patients and their relationship with interleukin (IL)-17, IL-23 and N-terminal propeptide of type III pro-collagen (PIIINP) as immune response mediators.
METHODS: The study was conducted on 50 Egyptian patients (36 male, 14 female) with hepatitis C virus (HCV) infection, who visited the Hepatology Outpatient Clinic in the Endemic Disease Hospital at Cairo University. Patients were compared with 25 age- and sex matched healthy individuals. Inclusion criteria were based on a history of liver disease with HCV genotype 4 (HCV-4) infection (as new patients or under follow-up). Based on ultrasonography, patients were classified into four subgroups; 14 with bright hepatomegaly; 11 with perihepatic fibrosis; 11 with hepatic cirrhosis; and 14 with cirrhosis and hepatocellular carcinoma (HCC). Total Vit D (i.e., 25-OH-Vit D) and active Vit D [i.e., 1,25-(OH)2-Vit D] assays were carried out using commercial kits. IL-17, IL-23 and PIIINP levels were assayed using enzyme linked immunosorbent assay kits, while HCV virus was measured by quantitative and qualitative polymerase chain reaction.
RESULTS: Levels of Vit D and its active form were significantly lower in advanced liver disease (hepatic cirrhosis and/or carcinoma) patients, compared to those with bright hepatomegaly and perihepatic fibrosis. IL-17, IL-23 and PIIINP levels were markedly increased in HCV patients and correlated with the progression of hepatic damage. The decrease in Vit D and active Vit D was concomitant with an increase in viral load, as well as levels of IL-17, IL-23 and PIIINP among all subgroups of HCV-infected patients, compared to normal healthy controls. A significant negative correlation was evident between active Vit D and each of IL-17, IL-23 and PIIINP ($r = -0.679, -0.801$ and -0.920 at $P < 0.001$, respectively). HCV-infected men and women showed no differences with respect to Vit D levels. The viral load was negatively correlated with Vit D and active Vit D ($r = -0.084$ and -0.846 at $P < 0.001$, respectively), and positively correlated with IL-17, IL-23 and PIIINP ($r = 0.951$, 0.922 and 0.94 at $P < 0.001$, respectively). Whether the deficiency in Vit D was related to HCV induced chronic liver disease or was a predisposing factor for a higher viral load remains to be elucidated.

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CONCLUSION: The negative correlations between Vit D and IL-17, IL-23 and PⅢNP highlight their involvement in the immune response in patients with HCV-4- related liver diseases in Egypt.

25OH Vitamin D was measured with the Medgenix (now DIAsource) 25OH Vitamin D Total RIA assay (KIP1971).

- BONAKDARAN S. (2012)

The Effects of Calcitriol on Albuminuria in Patients with Type-2 Diabetes Mellitus. Saudi J Kidney Dis. Transpl., 23(6):1215-1220

The renin–angiotensin system has a major role in the development of diabetic nephropathy (DN). It is reported that vitamin D analogues are able to suppress renin excretion. Thus, this study was conducted to determine whether there is any correlation between albuminuria as a marker of DN with vitamin D levels in diabetic patients. Also, an assessment was made on the effects of vitamin D therapy on albuminuria in this group of patients. We conducted this cross-sectional study on 119 outpatients with type-2 diabetes. The serum levels of 25-hydroxy vitamin D [25 (OH) D] and the albumin to creatinine ratio were assessed in all the study patients. Patients with vitamin D deficiency/insufficiency received calcitriol therapy for eight weeks, following which the laboratory tests were repeated. The mean age of the study patients was 55.3 ± 11.2 years, 43 (36.13%) had vitamin D insufficiency [25 (OH) D <25 ng/mL] and 31 (26.1%) had vitamin D deficiency [25 (OH) D <15 ng/mL]. We found a significant correlation between 25 (OH) D levels and presence of microalbuminuria (P = 0.04) in patients with vitamin D deficiency. Therapy with calcitriol had a beneficial effect on the albumin excretion rate, although this change was not significant (P = 0.22). However, the effects of calcitriol on reduction of diastolic blood pressure (P = 0.004), glycosylated hemoglobin (P = 0.014) and levels of total cholesterol (P = 0.019), low-density lipoprotein (0.04) and high-density lipoprotein (P = 0.001) was significant. Our study suggests that vitamin D deficiency has a negative effect on albuminuria in diabetic patients, and its replacement may be associated with a beneficial effect on the risk factors of DN, such as hyperlipidemia and hypertension.

25OH Vitamin D was measured with one of the BioSource Europe (now DIAsource) 25OH Vitamin D RIA assay (KIP1961 or KIP1971).

- FICHNA M. (2012)

Increased serum osteoprotegerin in patients with primary adrenal insufficiency receiving conventional hydrocortisone substitution.
Journal of Physiology and Pharmacology, 63(6):677-682

Patients treated for primary adrenal insufficiency (PAI) are at risk of steroid over-replacement, which may affect their skeleton. The study was aimed to investigate the effect of steroid substitution on serum osteoprotegerin and receptor activator of nuclear factor kappa-beta ligand (RANKL) levels in relation to bone mineral density (BMD) in PAI. Eighty patients (mean age 47.2±14.5 years, mean hydrocortisone dose 0.49±0.14 mg/kg/day) and 63 healthy subjects were included. Serum osteoprotegerin, RANKL, 25-hydroxyvitamin D3, calcium, phosphate, alkaline phosphatase, intact parathormone, and dehydroepiandrosterone-sulfate levels were evaluated in patients and controls. BMD was assessed in affected subjects using dual-energy X-ray absorptiometry. Mean osteoprotegerin concentration in PAI patients appeared significantly higher vs. controls (p=0.002), while RANKL levels were similar (p=0.430). Serum osteoprotegerin increased with age (p<0.001), but showed no correlation with daily hydrocortisone dose. Osteoprotegerin was negatively correlated with serum dehydroepiandrosterone-sulfate (p=0.008) and with BMD at the lumbar spine (p<0.001) and femoral neck (p=0.003). RANKL correlated negatively with PAI duration (p=0.029) and positively with daily hydrocortisone dose (p=0.018). Lumbar spine osteoporosis and osteopenia were found in 12 and 31

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patients, respectively, whereas in femoral neck: in 5 and 33 individuals. Patients with osteoporosis displayed higher osteoprotegerin levels, but after the age-adjustment the correlation was lost. In conclusion, increased osteoprotegerin in PAI might reflect a compensatory response to enhanced bone resorption due to exogenous steroid excess and/or result from a deficit in adrenal androgens. RANKL levels remain within normal range on standard steroid replacement.

25OH Vitamin D was measured with the DIAsource 25OH Vitamin D3 RIA assay (KIP1961).

- ESCUDER P.T. (2012)

Fibroblast growth factor 23 (FGF 23) and phosphocalcic metabolism in chronic kidney disease.
Nefrologia, 32(5):647-654

Background and Objectives: The ample information available in relation to FGF 23, calcium, phosphorus, PTH, and 25/1,25 vitamin D has allowed us to define consistent values for each variable in each stage of chronic kidney disease (CKD). These values can define early stages, prognostic issues, and new treatment targets. We describe a cross-sectional study of these parameters in patients with different stages of CKD.
Method: We measured FGF 23 by ELISA (intact molecule, Kainos Laboratory, Japan), calcium, phosphorus, PTH and vit D by standard methods.
Results: We examined 251 patients, 146 of which were men, with a mean age of 62.5 (11.5) years and 43% prevalence of type II DM. Levels of FGF 23 rose progressively, in a very significant manner, in correlation with the evolution of CKD, especially in stage 4 as compared to stage 1 (110.61ng/L vs 31.32ng/L). The same happened with iPTH values. Additionally, levels of 1,25 vitamin D decreased in a similar manner. Calcium values did not change. 25 vit D3 levels were low at all times and showed no tendency for a steady decline. Phosphorus rose in stage 4 CKD. Levels of FGF 23 were negatively correlated with renal function indicators and positively correlated with PTH and P. Conclusions: During the evolution of CKD, changes of FGF 23 and PTH would be the earliest markers. Calcium and 25 vit D3 do not vary with changes in the progression of CKD. Values of FGF 23 show an important correlation with PTH, 1,25 vit D3, P and estimated glomerular filtration rate.

1,25$(OH)_2$ Vitamin D was measured with the DIAsource 1,25$(OH)_2$ Vitamin D RIA assay (KIP1929).

- SUTTORP M. (2012)

Changes in bone metabolic parameters in children with chronic myeloid leukemia on imatinib treatment.
Med. Sci Monit., 18(12):CR721–CR728

Background: Imatinib is a highly effective drug in up-front treatment of chronic myeloid leukemia (CML). In children impaired longitudinal growth has been reported as side effect exerted by this drug under prolonged therapy. We therefore prospectively evaluated alterations of bone biochemical markers in pediatric patients with CML under ongoing imatinib exposure.
Material/Methods: Bone metabolic markers (calcium, phosphate, magnesium, parathyroid hormone, vitamin D, procollagen type l N propeptide [PINP], and C-terminal cross-linking telopeptide of collagen [CTX-I], osteocalcin [OC]; pyridinoline [PYD], and desoxypyridinoline [DPD]) were determined in 17 patients with CML aged 4–17 years under imatinib treatment in three-month intervals over a 2.5 year period.
Results: Hyperparathyroidism developed in 8/17 patients and low 25-hydroxyvitamin-D3 levels were found in 15/17 patients. Increased OC levels were detected in 58% of all specimen showing a linear

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significant decline of −0.30 µg OC per l per week (p=0.04). Serum PINP was lowered in 25% and serum CTX-I was above the normal range in 57% of the specimen originating exclusively from prepupertal patients. Urine PYD and Urine DPD levels were above the normal range in 10% and 9%, respectively, of all specimen collected and a statistically significant linear decline of −0.16 nmol DPD/mg creatinine/week was calculated (p=0.01).
Conclusions: Bone remodeling may be dysregulated by imatinib. Data suggest that impaired bone formation exceeds that of decreased bone resorption. Regular evaluation of the skeletal actions during long-term imatinib treatment in childhood CML is warranted.

$1,25(OH)_2$ Vitamin D was measured with the DIAsource $1,25(OH)_2$ Vitamin D RIA assay (KIP1929).

- KOH J.H. (2012)

25-Hydroxyvitamin D Status Based on Estimated Glomerular Filtration Rate in Patients with Chronic Kidney Disease.
Korean J Med., 83(6):740-751

Background/Aims: Accumulating data suggest that vitamin D deficiency is prevalent in patients with chronic kidney disease(CKD). However, comprehensive data are lacking for Koreans. The aim of this study was to survey vitamin D deficiency among patients with CKD in Korea and to identify the relationships among various factors.
Methods: We conducted a retrospective cohort study of 444 patients who were divided into four subgroups by estimated glomerular filtration rate (eGFR) for comparisons of mean 25-hydroxyvitamin D [25(OH)D] level and other parameters. In addition, non-dialyzed patients were categorized into four groups based on 25(OH)D levels (<10, 10-19, 20-29, and ≥ 30 ng/mL),and risk factors for severe vitamin D deficiency (<10 ng/mL) were investigated.
Results: Of patients with an eGFR ≥ 60 mL/min/1.73 m2, 43% (34/79) showed severe 25(OH)D deficiency, and the mean25(OH)D level was 11.7 ± 5.3 ng/mL. In CKD3 group, 53.2% (41/77) showed severe 25(OH)D deficiency, with a mean level of11.3 ± 7.2 ng/mL. In CKD4 group, 53.3% (49/92) had severe 25(OH)D deficiency, with a mean level of 11.0 ± 6.2 ng/mL. Approximately 71% (139/196) of patients in CKD5 group showed severe deficiency, and the mean level was 9.2 ± 5.9 ng/mL. Severe 25(OH)D deficiency was affected by winter season, renal function, diabetes, and low-density lipoprotein cholesterol. The serum parathyroid hormone level was inversely correlated with the 25(OH)D level, such that 25(OH)D < 20 ng/mL were associated with a steep increase in parathyroid hormone.
Conclusions: Vitamin D deficiency is highly prevalent in the Korean population. Few patients met a sufficient 25(OH)D concentration, even in the early stages of CKD. Our data suggest that 25(OH)D level of 20 ng/mL is a threshold for a rapid increase in parathyroid hormone levels.

25OH Vitamin D was measured with the DIAsource 25OH Vitamin D3 RIA assay (KIP1961).

- MARCÉN R. (2012)

Are low levels of 25-hydroxyvitamin D a risk factor for cardiovascular diseases or malignancies in renal transplantation?
Nephrol. Dial. Transplant., 27(Suppl. 4):iv47–iv52

Background. Observational studies in healthy people suggest an inverse relationship between 25-hydroxyvitamin D (25(OH)D levels) and cardiovascular diseases and malignancies. We performed an observational prospective study in renal transplant recipients to investigate the effects of vitamin D deficiency on cardiovascular and malignancy risks.

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Methods. From 389 renal transplant recipients, 331 with a functioning graft at 12 months were included in the study. Mineral metabolism parameters were measured at 1, 3, 4 and 12 months. Information regarding the cardiovascular events and malignancies were collected from an electronic database.
Results. According to the 1-year mean of 25(OH)D levels, 75 recipients (22.7%) had a normal vitamin D status, 161 (48.6%) had insufficiency and 95 (28.7%) had deficiency in vitamin D levels. During the follow-up, 80 recipients presented at least one cardiovascular event. The total cardiovascular diseases included: 27 patients with coronary diseases, 25 with cardiac failure, 18 with arrhythmia, 11 with acute cerebrovascular events and 19 with peripheral vascular disease. Cardiovascular events were not associated with 25(OH)D levels or vitamin D status, and the 10-year cumulative incidence was 29.3% for normal vitamin D status and 31.6% for insufficiency and 51.9% for deficiency (P = 0.216). Furthermore, Cox univariate analysis showed no association between cardiovascular events and vitamin D levels or vitamin D status. In addition, 53 recipients presented at least one malignancy: 33 non-melanoma skin malignancies and 20 nonskin malignancies (5 prostate, 3 kidney and urinary tract, 2 colon, 2 lung, 2 lymphoma, 2 breast and 4 from other locations). The cumulative incidence of malignancies was 21.3% for normal vitamin D status, 22.7% for insufficiency and 16.7% for deficiency (P = 0.818).
Conclusions. Our data suggested that low vitamin D levels were not associated with an increased risk of cardiovascular diseases or malignancies. However, due to the small number of patients and events, the results should not be considered as definitive. Additional studies with a higher number of patients are required to elucidate the true impact of vitamin D status on cardiovascular and malignancy risks.

$1,25(OH)_2$ Vitamin D was measured with the BioSource Europe (now DIAsource) $1,25(OH)_2$ Vitamin D RIA assay (KIP1929).

- SZYMCZAK J. (2012)
Low bone mineral density in adult patients with coeliac disease.
Polish Journal of Endocrinology, 63(4):270-276

Introduction: Calcium and vitamin D malabsorption in coeliac disease (CD) predispose to skeletal demineralization. The aim of this study was to evaluate the prevalence of bone mineral density (BMD) and calcium deficiencies in adult patients with CD and assess whether a gluten-free diet is sufficiently effective for BMD restoration.
Material and methods: BMD and biochemical parameters of bone and mineral metabolism were measured in 35 adult CD patients receiving (19) or not receiving (16) a gluten-free diet (GFD) and in 36 controls. Then the CD patients were treated with a GFD and calcium (1.0 g/day) plus alfacalcidol (0.25–1 μg/day) for one year.
Results: Reduced BMD was diagnosed in 57–77% of the patients. Mean calcaemia, calciuria, and 25(OH) vitamin D were lower, but serum PTH and bone-turnover markers (ALP, osteocalcin, ICTP) were significantly higher in the CD patients than in the controls. In the patients on the diet (GFD(+)), BMD was higher than in the GFD(–) patients, but lower than in the controls. The biochemical parameters were normal in the GFD(+) patients except for diminished calciuria. Mean BMD after one year of treatment significantly increased ($p < 0.05$), mostly in the lumbar spine (mean: 7.3%), but decreased in five patients who did not strictly adhere to the GFD.
Conclusions: Deficiencies in calcium, vitamin D, and BMD are very common in adult CD patients. Gluten avoidance increased BMD, although the values remained markedly lower in several patients. Because of chronic calcium deficiency despite GFD, calcium and vitamin D supplementation in most adult CD patients is proposed.

$1,25(OH)_2$ Vitamin D and 25OH Vitamin D were respectively measured with the BioSource Europe (now DIAsource) $1,25(OH)_2$ Vitamin D RIA assay (KIP1929) and 25OH Vitamin D3 RIA assay (KIP1961).

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- GRUSON D. (2013)

Measurement of 25-hydroxyvitamin D: evaluation of the new DIAsource ELISA assay.
Endocrine Abstracts, 32:P148

Background: Vitamin D is an important contributor to musculoskeletal health and its potential involvement has recently been underlined in several non-skeletal diseases. Measurement of circulating levels of 25-hydroxyvitamin D (25OHD) represents the most reliable assessment of vitamin D status. Several assays are available but are not commutable because of a lack of of standardization. The aim of our study was to evaluate the performance of a new ELISA for measurement of 25OHD levels.
Methods: 25OHD levels were measured with a newly released ELISA (Diasource Immunoassays), a simplified method without pre-treatment step. Method comparison was performed using 199 patients' samples with automated chemiluminescent immunoassay commonly used in clinical laboratories (Liaison, DiaSorin).
Results: According to our automated assay routine cut-points, serum concentrations of 25OHD were below 20 ng/ml in 96 patients, between 20 and 30 ng/ml in 68 patients and above 30 ng/ml in 35. The ELISA and the automated methods were significantly correlated (r=0.9230; P<0.0001) and the Passing and Bablock regression analysis showed a slope of 1.218 (95% CI: 1.1434 to 1.2944) and an intercept of −1.8775 ng/ml (95% CI −3.2694 to −0.3363). A small negative difference (2.7905 ng/ml; 95% CI −3.4546 to −2.1265) was highlighted, for the ELISA method through the Bland and Altman plot and important discrepancies (higher than 10 ng/ml) were observed in 12 samples.
Conclusions: Our preliminary results showed that the new 25OHD ELISA assay demonstrated a good agreement with a commonly used assay. A small difference was evidenced but its clinical impact is limited. However, additional investigations will be required to confirm the performances of this new simplified ELISA assay.

- LARIJANI B. (2013)

The Relation between Serum Vitamin D Levels and Blood Pressure: A Population-Based Study.
Acta Medica Iranica, 52(4):290

Vitamin D deficiency has been proposed as an associating factor with increased blood pressure. We studied the relationship between serum vitamin D and blood pressure in a large representative sample of Iranian population. In this cross-sectional study, based on the data of 2508 adults (aged between 20 and 70 years) from the Iran Multicenter Osteoporosis Study (IMOS), the association between serum vitamin D and blood pressure was investigated. There was a significant difference between mean (±SD) vitamin D levels of the individuals with stage I hypertension and that of the three other groups (Normal: 32.9 (±27.5); Prehypertension: 34.4 (±27.2); Stage-I: 38.7 (±29.2); Stage-II: 34.7 (±24.0) ng/ml; P<0.05. In multivariate regression models, the weak positive association of vitamin D and systolic blood pressure values disappeared after age and Body Mass Index (BMI) adjustment. We found a statistically positive but weak association between vitamin D serum concentration and systolic blood pressure. Considering the difference noted between our results and previous studies, further research is needed to assess the potential effect of ethnicity and genetic factors on these findings.

25OH Vitamin D was measured with one of the BioSource Europe (now DIAsource) 25OH Vitamin D RIA assay (KIP1961 or KIP1971).

- CRAVER L. (2013)

A low fractional excretion of Phosphate/Fgf23 ratio is associated with severe abdominal Aortic calcification in stage 3 and 4 kidney disease patients.

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BMC Nephrology, 14:221

Background: Vascular calcification (VC) contributes to high mortality rates in chronic kidney disease (CKD). High serum phosphate and FGF23 levels and impaired phosphaturic response to FGF23 may affect VC. Therefore, their relative contribution to abdominal aortic calcification (AAC) was examined in patients CKD stages 3–4.
Methods: Potential risk factors for AAC, measured by the Kauppila Index (KI), were studied in 178 patients.
Results: In multivariate linear analysis, AAC associated positively with age, male gender, CKD-stage, presence of carotid plaques (CP) and also with FGF23, but negatively with fractional excretion of phosphate (FEP). Intriguingly, FEP increased with similar slopes with elevations in PTH, with reductions in GFR, and also with elevations in FGF23 but the latter only in patients with none (KI = 0) or mild (KI = 1-5) AAC. Lack of a FEP-FGF23 correlation in patients with severe AAC (KI > 5) suggested a role for an impaired phosphaturic response to FGF23 but not to PTH in AAC. Logistic and zero-inflated analysis confirmed the independent association of age, CKD stage, male gender and CP with AAC, and also identified a threshold FEP/FGF23 ratio of 1/3.9, below which the chances for a patient of presenting severe AAC increased by 3-fold. Accordingly, KI remained unchanged as FEP/FGF23 ratios decreased from 1/1 to 1/3.9 but markedly increased in parallel with further reductions in FEP/FGF23 < 1/3.9.
Conclusions: In CKD 3–4, an impaired phosphaturic response to FGF23 with FEP/FGF23 < 1/3.9 associates with severe AAC independently of age, gender or CP.

25OH Vitamin D was measured with the BioSource Europe (now DIAsource) 25OH Vitamin D3 RIA assay (KIP1961).

- DEMIR M. (2013)

The Relationship between Vitamin D Deficiency and Pulmonary Hypertension.
Prague Medical Report, 114(3):154–161

Vitamin D deficiency actives renin-angiotensin-aldosterone system (RAAS) which affects cardiovascular system. Activation of RAAS is associated with pulmonary hypertension (PHT). Relation between vitamin D deficiency and PHT could be therefore suggested. In our study we compared pulmonary artery pressure between vitamin D deficiency and control groups. 115 consecutive patients (average age: 61.86 ± 5.86) who have detected very low vitamin D (vitamin D levels < 10 ng/ml) were enrolled. 117 age matched persons (average age: 61.74 ± 5.99) were selected as the control group. All groups underwent transthoracic echocardiography. Routine biochemical measurement of 25-OH vitamin D and parathormon (PTH) levels were performed. Baseline characteristics of the study groups were comparable. Systolic pulmonary artery pressure (SPAP) of patients in the low vitamin D group was higher than the control groups. As a result our study, a relation between vitamin D deficiency and pulmonary artery hypertension was revealed.

25OH Vitamin D was measured with the BioSource Europe (now DIAsource) 25OH Vitamin D3 RIA assay (KIP1961).

- DEMIR M. (2013)

Vitamin D levels in patients with chronic hepatitis B virus infection and naturally immunized individuals.
Internal Medicine Inside, 1:2

Vitamin D deficiency is associated with several adverse health outcomes, and vitamin D appears to have systemic antimicrobial effects that may be crucial in a variety of both acute and chronic illnesses.

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In the present study, 25-hydroxyvitamin D (25-OHD) levels were compared among patients with chronic hepatitis B virus infection, naturally immunized individuals and control individuals. Thirty-five patients with chronic hepatitis B virus infection (group I), 30 naturally immunized individuals (group II) and 30 healthy adults were included in the present study. Markers of hepatitis were measured using commercially available kits based on chemiluminescence assays. Routine biochemical parameters, hepatitis B virus serology, hepatitis B virus DNA, 25-OHD and parathyroid hormone levels were measured. Baseline characteristics of the study groups were comparable. Patients in group I had a lower 25-OHD level compared with group II and the control group (7.65±4.19 ng/mL versus 12.1±7.13 ng/mL and 14.17±9.18 ng/mL, respectively; P<0.001). In addition, patients in group I had a higher parathyroid hormone level compared with group II and the control group (88.21±34.2 ng/mL versus 75.14±23.4 ng/mL and 74.16±20.15 ng/mL, respectively; P=0.001). 25-OHD levels were correlated with hepatitis B virus DNA levels. In patients infected with hepatitis B virus, diminished 25-OHD levels may be an indicator of the status of viral replication and portends a poor prognosis.

25OH Vitamin D was measured with the BioSource Europe (now DIAsource) 25OH Vitamin D3 RIA assay (KIP1961).

- DEMIR M. (2013)

Relationship Between Vitamin D Deficiency and Nondipper Hypertension. Clinical and Experimental Hypertension, 35(1):45–49

Nondipper hypertension is associated with increased cardiovascular morbidity and mortality. Vitamin D deficiency is associated with cardiovascular diseases such as coronary artery disease, heart failure, and hypertension. Vitamin D deficiency activates the renin–angiotensin–aldosterone system, which affects the cardiovascular system. For this reason, a relationship between vitamin D deficiency and nondipper hypertension could be suggested. In this study, we compared 25-OH vitamin D levels between dipper and nondipper hypertensive patients. The study included 80 hypertensive patients and they were divided into two groups: 50 dipper patients (29 male, mean age 51.5 8 years) and 30 nondipper patients (17 male, mean age 50.6 5.4 years). All the patients were subjected to transthoracic echocardiography and ambulatory 24-hour blood pressure monitoring. In addition to routine tests, 25-OH vitamin D and parathormone (PTH) levels were analyzed. All the patients received antihypertensive drug therapy for at least 3 months prior to the evaluations. 25-OH vitamin D and PTH levels were compared between the two groups. No statistically significant difference was found between the two groups in terms of basic characteristics. The average PTH level of hypertensive dipper patients was lower than that of nondipper patients (65.3 14.2 vs. 96.9 30.8 pg/mL, P < .001). The average 25-OH vitamin D level of hypertensive dipper patients was higher than that of nondipper patients (21.9 7.4 vs. 12.8 5.9 ng/mL, P ¼ .001). The left ventricular mass and left ventricular mass index were lower in the dipper patients than in the nondipper patients (186.5 62.1 vs. 246.3 85.3 g, P ¼ .022; and 111.6 21.2 vs.147 25.7 g/m2 , P < .001, respectively). Other conventional echocardiographic parameters were similar between the two groups. Daytime systolic and diastolic blood pressure measurements were similar between dippers and nondippers, but there was a significant difference between the two groups with regard to nighttime measurements (nighttime systolic 118.5 5.8 vs.130.2 9.6 mm Hg, P < .001; and nighttime diastolic 69.3 4.8 vs.78.1 7.2 mm Hg, P < .001, respectively). Our results suggest that vitamin D deficiency has a positive correlation with blood pressure and vitamin D deficiency could be related to nondipper hypertension. The measurement of vitamin D may be used to indicate increased risk of hypertension-related adverse cardiovascular events.

25OH Vitamin D was measured with the BioSource Europe (now DIAsource) 25OH Vitamin D3 RIA assay (KIP1961).

- TALAEI A. (2013)

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The effect of vitamin D on insulin resistance in patients with type 2 diabetes. Diabetology & Metabolic Syndrome, 5:8

Introduction: Over the past decade, numerous non-skeletal diseases have been reported to be associated with vitamin D deficiency including type2 diabetes mellitus (T2DM). Different studies provide evidence that vitamin D may play a functional role in glucose tolerance through its effects on insulin secretion and insulin sensitivity. This study evaluates the effects of vitamin D supplementation on insulin resistance in T2DM.
Method: Through a before-after study, 100 patients with T2DM, 30–70 years old, were recruited from an Arak diabetes clinic as consecutive attenders. Participants were assessed for clinical and biochemistry. Serum insulin and, 25(OH)D concentration, and HOMA-IR was calculated. All measurements were performed at the beginning and the end of the study. Patients received 50,000 unit of vitamin D3 orally per week for eight weeks, Statistical analysis was made using SPSS17. The results were analyzed by descriptive tests, and a comparison between variables were made using paired T-tests or Wilcoxon tests, as appropriate.
Results: 100 participants including 70 women (70%) and 30 men (30%) took part in the study. All results were presented as Mean±SD, or medians of non-normally distributed. 24% of the participants were Vitamin D deficient {serum 25(OH)D ≤ 20 ng/ml(50 nmol/l)}. Mean serum 25 (OH) D concentration was 43.03± 19.28 ng/ml (107.5±48.2 nmol/l). The results at baseline and at the end, for FPG were 138.48±36.74 and 131.02±39 mg/dl (P=0.05), for insulin, 10.76±9.46 and 8.6±8.25 µIu/ml (P=0.028) and for HOMA-IR, 3.57±3.18 and 2.89±3.28 (P=0.008) respectively.
Conclusion: Our data showed significant improvements in serum FPG, insulin and in HOMA-IR after treatment with vitamin D, suggested that vitamin D supplementation could reduce insulin resistance in T2DM.

25OH Vitamin D was measured with one of the BioSource Europe (now DIAsource) 25OH Vitamin D RIA assay (KIP1961 or KIP1971).

- JEON I.-H. (2013)

The Effect of Short-Term Low-Energy Ultraviolet B Irradiation on Bone Mineral Density and Bone Turnover Markers in Postmenopausal Women with Osteoporosis: A Randomized Single-Blinded Controlled Clinical Trial.
Srp Arh Celok Lek., 141(9-10):615-622

Introduction The importance of vitamin D on bone health and osteoporosis was studied by many researchers. The main role of the Vitamin D is to absorb calcium and phosphate and increase bone mineralization. Older people are at an increased risk of the inadequate vitamin D production in the skin because of lower sun exposure and reduced ability of the skin to synthesize vitamin D.
Objective The aim of this clinical trial was to evaluate the efficacy and tolerability of short-term (2 weeks) low energy UVB irradiation in postmenopausal women with osteoporosis using bone mineral density and bone turnover markers.
Methods A three-month, single-blinded, randomized, placebo-controlled clinical trial was conducted at the University hospital in Daegu, Republic of Korea. Fifty-two postmenopausal Korean women (older than 65 years) with osteoporosis were randomly allocated to have either low energy UVB or placebo for 30 minutes a day for two weeks of treatment during winter. Laboratory analysis and physical examination before and 4, 8 and 12 weeks after treatment were carried out and BMD was measured before and 8 and 12 weeks after treatment. The effects of time and treatment interaction between these two groups were evaluated by repeated-measure two-factor analysis, and subgroup analysis was performed to examine UVB effect on the vitamin D insufficient group [serum 25(OH)D3 concentration <30 ng/mL].
Results In vitamin D insufficient group, the effect of UVB irradiation on vitamin D and bone ALP as well as additional benefit on bone formation was confirmed. The vitamin D insufficient group showed

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statistically significant increment in serum 25(OH)D3 compared with the normal group (p<0.05). However, there was no significant difference between two groups in the other bone turnover markers, such as serum calcium, PTH-C, serum osteocalcin, serum CTX and BMD.
Conclusion Low-energy-short-term UVB radiation for postmenopausal women may be of use in vitamin D synthesis. There was a modest benefit in change of bone ALP especially in women with the insufficient vitamin D.

25OH Vitamin D was measured with one of the BioSource (now DIAsource) 25OH Vitamin D3 RIA assay (KIP1961).

- PAL M. (2013)

Comparison between different methods of estimation of vitamin D.
Advances in Biological Chemistry, 3:501-504

In order to determine the better method for detecting vitamin D status, we have estimated blood vitamin D in three methods such as high-pressure liquid chromatography, chemiluminescent immunoassays and enzyme immunoassays.
Method: Two hundred and sixteen subjects irrespective of age and sex were studied for blood vitamin D in all the three methods over a period of 2 years.

25OH Vitamin D was measured with the DIAsource 25OH Vitamin D Total ELISA assay (KAP1971).

- JANSEN E. (2013)

Biomarker measurements in the aging cohorts of the FP7 project "CHANCES".
Poster presentation at the Symposium "Biomarkers of Ageing" 2013, Konstanz, Germany, 22-23 March 2013 (http://www.chancesfp7.eu/events/Konstanz.pdf).

CHANCES (Consortium on Health and Ageing: Network of Cohorts in Europe and the United States) is a collaborative large-scale integrating project funded by the European Commission within the 7th Framework Program. The CHANCES project aims at combining and integrating on-going studies in order to produce evidence on ageing-related health characteristics and determinants in Europe. The CHANCES project focuses on four groups of chronic diseases and conditions which are major contributors to the burden of disease in the elderly: Cancer, Cardiovascular diseases and diabetes, Osteoporosis and fractures, Cognitive disorders.

25OH Vitamin D was measured with the DIAsource 25OH Vitamin D Total ELISA assay (KAP1971).

- AYGENCEL G. (2013)

Is Vitamin D Insufficiency Associated with Mortality of Critically Ill Patients ?
Critical Care Research and Practice, Article ID 856747

Objective. To evaluate the vitamin D status of our critically ill patients and its relevance to mortality. Patients and Methods. We performed a prospective observational study in the medical intensive care unit of a university hospital between October 2009 and March 2011. Vitamin D levels were measured and insufficiency was defined as <20 ng/mL. Results. Two hundred and one patients were included in the study. The median age was 66 (56–77) and the majority of patients were male (56%). The median serum level of vitamin D was 14,9 ng/mL and 139 (69%) patients were vitamin D insufficient on admission. While we grouped the ICU patients as vitamin D insufficient and sufficient, vitamin D

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insufficient patients had more severe acute diseases and worse laboratory values on admission. These patients had more morbidities and were exposed to more invasive therapies during stay. The mortality rate was significantly higher in the vitamin D insufficient group compared to the vitamin D sufficient group (43% versus 26%, P = 0, 027). However, logistic regression analysis demonstrated that vitamin D insufficiency was not an independent risk factor for mortality.
Conclusion. Vitamin D insufficiency is common in our critically ill patients (69%), but it is not an independent risk factor for mortality.

25OH Vitamin D was measured with one of the DIAsource 25OH Vitamin D RIA assay (KIP1961 or KIP1971).

- BIKLE D. (2013)

Variability in free 25(OH) vitamin D levels in clinical populations.
J. Steroid Biochem. Mol. Biol., S0960-0760.

Relationships between total and free 25(OH)D vary with clinical conditions that affect circulating protein concentrations, and may differ from predictions based on physiologic changes in circulating vitamin D binding protein and albumin. Direct measurement of free 25(OH) D warrants further evaluation to determine its clinical relevance in defining optimal vitamin D status for differing clinical conditions.

Free 25OH Vitamin D was measured with the Future Diagnostics Free 25OH Vitamin D ELISA assay which is exclusively distributed by DIAsource (KARF1991).

- PRATS M. (2013)

Effect of ferric carboxymaltose on serum phosphate and C-terminal FGF23 levels in non-dialysis chronic kidney disease patients: post-hoc analysis of a prospective study.
BMC Nephrol., 14:167

Background: Some parenteral iron therapies have been found to be associated with hypophosphatemia. The mechanism of the decrease in serum phosphate is unknown. The aim of this study is to examine the effect of IV ferric carboxymaltose(FCM) on phosphate metabolism and FGF23 levels in patients with chronic kidney disease(CKD).
Methods: This is a post-hoc analysis of a prospective study carried out in 47 non-dialysis CKD patients with iron-deficiency anaemia who received a single 1000 mg injection of FCM. Markers of mineral metabolism (calcium, phosphate, 1,25-dihydroxyvitamin D, PTH and FGF23[c-terminal]) were measured prior to FCM administration and at week 3 and week 12 after FCM administration. Based on the measured levels of serum phosphate at week 3, patiens were classified as hypophosphatemic or non-hypophosphatemic.
Results: Serum phosphate levels decreased significantly three weeks after FCM administration and remained at lower levels at week 12 (4.24 ± 0.84 vs 3.69 ± 1.10 vs 3.83 ± 0.68 mg/dL, respectively, p < 0.0001. Serum calcium, PTH and 1,25-dihydroxyvitamin D did not change over the course of the study. Serum FGF23 decreased significantly from 442(44.9-4079.2) at baseline to 340(68.5-2603.3) at week 3 and 191.6(51.3-2465.9) RU/mL at week 12, p < 0.0001. Twelve patients were non-hypophosphatemic and 35 hypophosphatemic. FGF23 levels decreased in both groups, whereas no changes were documented in any of the other mineral parameters.
Conclusions: In non-dialysis CKD patients, FCM induces reduction in serum phosphate levels that persists for three months. FCM causes a significant decrease in FGF23 levels without changes to other bone metabolism parameters.

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1,25(OH)$_2$ Vitamin D was measured with the DIAsource 1,25(OH)$_2$ Vitamin D RIA assay (KIP1929).

- BOK Y.P. (2013)

Correlation between serum 25-hydroxyvitamin D levels and methicillin - resistant Staphylococcus aureus skin colonization in atopic dermatitis.
Allergy Asthma Respir. Dis., 1(2):138-143

Purpose: Bacterial infection with Staphylococcus aureus is a common complication of atopic dermatitis (AD) and involved in the worsening of this disease. Recent studies have revealed an increasing prevalence of community-associated methicillin-resistant S. aureus (MRSA) among patients with AD and the role of vitamin D in the immunopathogenesis of AD. We carried out a study to see whether levels of vitamin D correlate with MRSA skin colonization in AD.
Methods: Total 60 patients with AD aged between 3 months and 6 years old were enrolled. We measured disease severity using the Scoring Atopic Dermatitis (SCORAD) index, serum levels of 25-hydroxyvitamin D (25(OH)D), total immunoglobulin E levels, eosinophil cationic protein and bacterial colonization by skin swab and culture method.
Results: S. aureus was cultured in 20 patients of the total (33.3%). MRSA was comprised 35% of the S. aureus-positive group. SCORAD value was significantly higher in S. aureus-positive group. Serum levels(mean± standard deviation) of 25(OH)D were lower in MRSA group (22.6± 11.5 ng/mL) compared with those of methicillin-sensitive S. aureus group (31.3± 10.2 ng/mL) or S. aureus negative group (34.3± 15.8 ng/mL). But there was no statistically significant difference.
Conclusion: Our study shows that the serum levels of 25(OH)D were lower in MRSA group. But there was no statistically significant difference. Therefore further studies including large numbers of cases are necessary.

25OH Vitamin D was measured with the DIAsource 25OH Vitamin D3 RIA assay (KIP1961).

- SCHÖTTKER B. (2014)

Vitamin D and mortality: meta-analysis of individual participant data from a large consortium of cohort studies from Europe and the United States.
BMJ, 348:g3656

Objective: To investigate the association between serum 25-hydroxyvitamin D concentrations (25(OH)D) and mortality in a large consortium of cohort studies paying particular attention to potential age, sex, season, and country differences.
Design: Meta-analysis of individual participant data of eight prospective cohort studies from Europe and the US.
Setting: General population.
Participants: 26 018 men and women aged 50-79 years.
Main outcome measures: All-cause, cardiovascular, and cancer mortality.
Results: 25(OH)D concentrations varied strongly by season (higher in summer), country (higher in US and northern Europe) and sex (higher in men), but no consistent trend with age was observed. During follow-up, 6695 study participants died, among whom 2624 died of cardiovascular diseases and 2227 died of cancer. For each cohort and analysis, 25(OH)D quintiles were defined with cohort and subgroup specific cut-off values. Comparing bottom versus top quintiles resulted in a pooled risk ratio of 1.57 (95% CI 1.36 to 1.81) for all-cause mortality. Risk ratios for cardiovascular mortality were similar in magnitude to that for all-cause mortality in subjects both with and without a history of cardiovascular disease at baseline. With respect to cancer mortality, an association was only observed among subjects with a history of cancer (risk ratio, 1.70 (1.00 to 2.88)). Analyses using all quintiles

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suggest curvilinear, inverse, dose-response curves for the aforementioned relationships. No strong age, sex, season, or country specific differences were detected. Heterogeneity was low in most meta-analyses.
Conclusions: Despite levels of 25(OH)D strongly varying with country, sex, and season, the association between 25(OH)D level and all-cause and cause-specific mortality was remarkably consistent. Results from a long term randomised controlled trial addressing longevity are being awaited before vitamin D supplementation can be recommended in most individuals with low 25(OH)D levels.

25OH Vitamin D was measured with the DIAsource 25OH Vitamin D Total ELISA assay (KAP1971) in the following cohorts: HAPIEE Czech Republic, HAPIEE Poland and HAPIEE Lithuania.

- BUCCA C. (2014)

Severe vitamin D deficiency is associated with frequent exacerbations and hospitalization in COPD patients.
Respiratory Research, 15:131

Background: Acute exacerbations of COPD (AECOPD) are common and strongly influence disease severity and relative healthcare costs. Vitamin D deficiency is frequent among COPD patients and its contributory role in disease exacerbations is widely debated. Our aim was to assess the relationship of serum vitamin D levels with COPD severity and AECOPD.
Methods: Serum vitamin D (25-hydroxyvitamin D) levels were measured in 97 COPD patients and related to lung function, comorbidities, FEV1 decline, AECOPD and hospital admission during the previous year.
Results: Most patients (96%) had vitamin D deficiency, which was severe in 35 (36%). No significant relationship was found between vitamin D and FEV1 or annual FEV1 decline. No difference between patients with and without severe vitamin D deficiency was found in age, gender, BMI, smoking history, lung function, and comorbidities, apart from osteoporosis (60.9% in severe deficiency vs 22.7%, p = 0.001). In multiple logistic regression models, severe deficiency was independently associated with AECOPD [adjusted odds ratios (aOR) of 30.5 (95% CI 5.55, 168), p < 0.001] and hospitalization [aOR 3.83 (95% CI 1.29, 11.4), p = 0.02]. The odds ratio of being a frequent exacerbator if having severe vitamin D deficiency was 18.1 (95% CI 4.98, 65.8) (p < 0.001), while that of hospitalization was 4.57 (95% CI 1.83, 11.4) (p = 0.001).
Conclusions: In COPD patients severe vitamin D deficiency was related to more frequent disease exacerbations and hospitalization during the year previous to the measurement of vitamin D. This association was independent of patients' characteristics and comorbidities.

25OH Vitamin D was measured with the DIAsource 25OH Vitamin D Total RIA assay (KIP1971).

- AMANI R. (2014)

Comparison of Antioxidant Status and Vitamin D Levels between Multiple Sclerosis Patients and Healthy Matched Subjects.
Multiple Sclerosis International, 539854, 5 pages

Objective. The aim of the present study was to compare the serum levels of total antioxidant status (TAS) and 25(OH) D3 and dietary intake of multiple sclerosis (MS) patients with those of normal subjects.
Method. Thirty-seven MS patients (31 women) and the same number of healthy matched controls were compared for their serum levels and dietary intake of 25(OH) D3 and TAS. Sun exposure and the

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intake of antioxidants and vitamin D rich foods were estimated through face-to-face interview and food frequency questionnaire.
Results. Dietary intake of antioxidants and vitamin D rich foods, vitamin C, vitamin A, and folate was not significantly different between the two groups. There were also no significant differences in the mean levels of 25(OH) D3 and TAS between the study groups. Both groups had low serum levels of 25(OH) D3 and total antioxidants.
Conclusion. No significant differences were detected in serum levels and dietary intake of vitamin D and antioxidants between MS patients and healthy controls. All subjects had low antioxidant status and vitamin D levels.

25OH Vitamin D was measured with one of the BioSource Europe (now DIAsource) 25OH Vitamin D RIA assay (KIP1961 or KIP1971).

- KIM H.C. (2014)

Serum 25-Hydroxyvitamin D and Insulin Resistance in Apparently Healthy Adolescents.
PLoS ONE 9(7): e103108

Purpose: Vitamin D deficiency is a common condition that is associated with diabetes and insulin resistance. However, the association between vitamin D and insulin resistance has not been fully studied, especially in the general adolescent population. Therefore, we assessed the association between serum 25-hydroxyvitamin D [25(OH)D] level and insulin resistance among apparently healthy Korean adolescents.
Methods: A total of 260 (135 male and 125 female) adolescents in a rural high school were assessed for serum 25(OH)D, fasting plasma glucose, and insulin. All of the participants were aged 15 to 16 years old, and without known hypertension or diabetes. Serum 25(OH)D was analyzed both as a continuous and categorical variable in association with insulin resistance. Insulin resistance was estimated by homeostasis model assessment (HOMA-IR). Increased insulin resistance was operationally defined as a HOMA-IR value higher than the sex-specific 75th percentile.
Results: In male adolescents, every 10 ng/ml decrease in 25(OH)D level was associated with a 0.25 unit increase in HOMA-IR (p = 0.003) after adjusting for age and BMI. Compared to those in the highest quartile, male adolescents in the lowest 25(OH)D quartile were at significantly higher risk for insulin resistance: unadjusted odds ratio 4.06 (95% CI, 1.26 to 13.07); age and BMI adjusted odds ratio 3.59 (95% CI, 1.03 to 12.57). However, 25(OH)D level, either in continuous or categorical measure, was not significantly associated with insulin resistance among female adolescents.
Conclusions: This study suggests that serum 25(OH)D level may be inversely associated with insulin resistance in healthy male adolescents.

25OH Vitamin D was measured with the DIAsource 25OH Vitamin D3 RIA assay (KIP1961).

- JOSHI A. (2014)

Vitamin D deficiency is associated with increased mortality in critically ill patients especially in those requiring ventilatory support.
Indian Journal of Endocrinology and Metabolism, 18(4):511

Introduction: Vitamin D (VitD) classically recognized for its role in the musculoskeletal system, has been implicated in myriad of conditions such as diabetes, immune dysfunction, cancers, heart disease, metabolic syndrome, etc. We studied the role of VitD in acute care setting and its correlation with mortality.
Materials and Methods: A total of 85 consecutive consenting patients admitted in medical

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intensive care unit of tertiary care hospital who fulfilled the inclusion criteria were included. All patients were evaluated clinically, and blood samples were collected for hemogram, biochemical investigations including serum calcium, phosphorus, alkaline phosphatase, magnesium, along with 25(OH) VitD, 1,25(OH) VitD and intact parathormone levels. Simplified acute physiology score (SAPS II) was calculated for all patients.
Results: VitD was deficient (<30 ng/ml) in 27 patients (32%). The overall mortality was more in VitD deficient group as compared to VitD sufficient group (74 vs. 41%; P < 0.05). The actual mortality in VitD deficient group was higher than the mortality predicted by SAPS II score (50 vs. 74%; P < 0.0507). VitD deficiency was also associated with more mortality among those requiring ventilator support (95% vs. 40%; P < 0.05) as well as with higher blood glucose (124.5 ± 29.7 vs. 94.8 ± 19.8: P < 0.01) levels.
Conclusion: VitD deficiency was associated with increased mortality, poor ventilator outcomes, and increased blood glucose in critically ill patients.

25OH Vitamin D was measured with the DIAsource 25OH Vitamin D3 RIA assay (KIP1961).

- HOSSEIN-NEZHAD A. (2014)

The Role of Vitamin D Deficiency and Vitamin D Receptor Genotypes on the Degree of Collateralization in Patients with Suspected Coronary Artery Disease.
BioMed Research International, ID 304250, 8 pages

We determined the association of vitamin D deficiency and the FokI polymorphism of the vitamin D receptor (VDR) gene in 760 patients who underwent angiography due to suspected coronary artery disease (CAD). Angiography and the Rentrop scoring system were used to classify the severity of CAD in each patient and to grade the extent of collateral development, respectively. Polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) was used to determine the FokI VDR gene polymorphism. The prevalence of severe vitamin D deficiency (serum 25(OH)D < 10 ng/mL) was significantly higher in patients with at least one stenotic coronary artery compared to those without any stenotic coronary arteries. Severe vitamin D deficiency was not independently associated with collateralization, but it was significantly associated with the VDR genotypes. In turn, VDR genotype was independently associated with the degree of collateralization; the Rentrop scores were the highest in FF, intermediate in Ff, and the lowest in the ff genotype. The results show that FokI polymorphism is independently associated with collateralization. Additionally, vitamin D deficiency is more prevalent in patients with CAD that may result from FokI polymorphism. Therefore, maintaining a normal vitamin D status should be a high priority for patients with CAD.

25OH Vitamin D was measured with one of the BioSource (now DIAsource) 25OH Vitamin D RIA assay (KIP1961 or KIP1971).

- YENIOVA O. (2014)

The association of vitamin D deficiency with nonalcoholic fatty liver disease.
Clinics., 69(8):542-546

OBJECTIVE: Vitamin D deficiency has been related to diabetes, hypertension, hyperlipidemia and peripheral vascular disease. In this study, we aimed to investigate the role of vitamin D status in non-alcoholic fatty liver disease.
METHODS: We included 211 consecutive subjects to examine the presence of non-alcoholic fatty liver disease. Of these subjects, 57 did not have non-alcoholic fatty liver disease and 154 had non-alcoholic fatty liver disease.
RESULTS: The non-alcoholic fatty liver disease group had significantly higher fasting blood glucose (p = 0.005), uric acid (p = 0.001), aspartate aminotransferase (p,0.001), alanine aminotransferase

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(p,0.001), c-glutamyltransferase (p,0.0001), alkaline phosphatase (p = 0.028), HbA1c (p,0.001), ferritin (p,0.001), insulin (p = 0.016), C-peptide (p = 0.001), HOMA-IR (p = 0.003), total cholesterol (p = 0.001), triglyceride (p = 0.001) and white blood cell (p = 0.04) levels. In contrast, the non-alcoholic fatty liver disease group had significantly lower 25(OH)D levels (12.3¡8.9 ng/dl, p,0.001) compared with those of the control group (20¡13.6 ng/dl).
CONCLUSIONS: In this study, we found lower serum 25(OH)D levels in patients with non-alcoholic fatty liver disease than in subjects without non-alcoholic fatty liver disease. To establish causality between vitamin D and non-alcoholic fatty liver disease, further interventional studies with a long-term follow-up are needed.

25OH Vitamin D was measured with the BioSource (now DIAsource) 25OH Vitamin D3 RIA assay (KIP1961).

- ABDELGADIR E.I.E. (2014)

Vitamin D Deficiency and Insufficiency in Patients Attending a General Hospital in Dubai, United Arab Emirates.
Ibnosina J. Med. B.S., 6(2):81-84

Background: Vitamin D deficiency is a common medical problem, especially in the gulf region of the Middle East. The prevalence in several studies has exceeded 50% and being more frequent among females.
Objective: We assessed the prevalence of vitamin D deficiency in patients attending a general hospital in both men and women in different age groups.
Methods: Vitamin D level data for patients who attended Dubai hospital in the period between 2008 and 2012 were examined retrospectively. The serum 25(OH) D levels were crosschecked in patients' charts and the laboratory electronic database. Patients with incomplete medical records, those already on treatment with vitamin D, and patients with contradicting results in the medical files and the electronic database has been excluded. Data were analysed using descriptive analysis relating vitamin D levels to age, gender, and ethnicity.
Results: The total number included was 2836 patients. 81% of them had 25 (OH) D levels of <30 ng/ml. About 76.4% (n=2166) of the studied group were females. There was no difference in prevalence between males and females. Arab ethnicity was associated with more marked vitamin D deficiency and less sufficiency.
Conclusion: We conclude that vitamin D deficiency is a considerably major health problem in the emirate of Dubai. Higher awareness among healthcare providers and the community is needed for screening and treatment necessity.

25OH Vitamin D was measured with one of the DIAsource 25OH Vitamin D RIA assay (KIP1961 or KIP1971).

- LONE K.P. (2014)

Vitamin D and cardiometabolic risk factors in adult non-diabetic offspring of type 2 diabetic parents.
J. Pak. Med. Assoc., 64(11):1229-1234

Objective: To measure serum vitamin D levels and assess its correlation with the various components of metabolic syndrome in adult non-diabetic offsprings of type 2 diabetics.
Methods: The analytical cross-sectional study was conducted from February to December 2012 at the Department of Physiology and Cell Biology, University of Health Sciences, Lahore. Data on anthropometric and physiologic/biochemical parameters was collected. Fasting blood samples were

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collected and serum was analysed for fasting serum insulin, fasting blood sugar, lipid profile and vitamin D. SPSS 20 was used for statistical analysis.
Results: Of the total 88 subjects in the study, 40(45.5%) were offsprings of type 2 diabetics and 48(54.5%) were offsprings of non-diabetic parents. Vitamin D deficiency (<20ng/ml) was observed in 86 (98.5%) of the subjects and 77 (87.5%) had vitamin D levels <15ng/ml. Severe deficiency (<10ng/ml) was seen in 61 (70%) subjects. Inverse correlation was observed between vitamin D and low density lipoprotein, total cholesterol, total cholesterol/high density lipoprotein ratio, Fasting Blood Sugar and homeostasis model assessment of insulin resistance.
Conclusion: The subjects were severely deficient in vitamin D and its levels were inversely correlated with most of the components of metabolic syndrome.

25OH Vitamin D was measured with the DIAsource 25OH Vitamin D Total ELISA assay (KAP1971).

- KIM H.C. (2014)

Association between Serum 25-Hydroxyvitamin D Level and Insulin Resistance in a Rural Population.
Yonsei Med. J., 55(4):1036-1041

Purpose: A low serum 25-hydroxyvitamin D [25(OH)D] level in the blood has been correlated with an increased risk of diabetes mellitus; however, the association between serum 25(OH)D level and insulin resistance has not been established in a Korean rural population. The aim of this study was to investigate the independent association between serum 25(OH)D level and insulin resistance in rural Korean adults.
Materials and Methods: This study used data from the Korean Genome Epidemiology Study-Kangwha Study. In the 2011 study, 1200 adults completed health examinations. In an ancillary study, serum 25(OH)D level was measured in a subsample (n=813). After excluding those taking vitamin D supplements, a cross-sectional analysis was carried out on 807 participants (324 men and 483 women) aged 40 to 89 years old. Measured from overnight fasting blood samples, glucose and insulin levels were used to calculate the homeostasis model assessment for insulin resistance (HOMA-IR). Measures of glucose, insulin, and HOMA-IR were log-transformed for parametric tests.
Results: Serum 25(OH)D level was inversely associated with HOMA-IR (β=-0.003, p=0.039) in a univariate analysis. However, the association was not significant after adjustment for sex and age (β=-0.002, p=0.123) or after adjustment for sex, age, body mass index, smoking status, alcohol intake, and regular exercise (β=-0.003, p=0.247).
Conclusion: Our findings suggest that vitamin D is not independently associated with insulin resistance in Korean men and women.

25OH Vitamin D was measured with one of the DIAsource 25OH Vitamin D RIA assay (KIP1961 or KIP1971).

- LEE S.-G. (2014)

Association between Vitamin D Deficiency and Carotid Intima-media Thickness in Patients with Rheumatoid Arthritis.
Journal of Rheumatic Diseases, 21(3):132-139

Objective. The present study determined if vitamin D deficiency is a potential risk factor for increased carotid intima-media thickness (CIMT) in patients with rheumatoid arthritis (RA).
Methods. This cross-sectional study analyzed 50 consecutive female RA patients without cardiovascular disease history at the Pusan National University Hospital between September and December of 2013. CIMT was measured using a high-resolution ultrasonography. Serum 25-hydroxy vitamin D (25-OHD) levels were assessed by radioimmunoassay, and vitamin D deficiency was defined

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as serum 25-OHD levels <20 ng/mL. Stepwise multivariable linear regression analyses were performed to evaluate the association between vitamin D deficiency and increased CIMT.
Results. The median 25-OHD level (inter-quartile range) was 14.0 (11.0–20.7) ng/mL, and 74% of patients had vitamin D deficiency. The mean±standard deviation of CIMT was 0.58±0.08 mm. RA patients with vitamin D deficiency had significantly higher CIMT than those without this feature (0.59±0.07 vs 0.54±0.05, p=0.028). In univariable linear regression models, vitamin D deficiency (β(SE)=0.047 (0.021), p=0.028), older age (β(SE)=0.003 (7.2-4), p <0.001) and higher disease activity score 28-erythrocyte sedimentation rate (β(SE)=0.021 (0.010), p=0.034) and Korean version of health assessment questionnaire score (β(SE)=0.051 (0.015), p=0.002) were significantly associated with increased CIMT. Vitamin D deficiency remained statistically significant in multivariable regression models after adjusting for confounders.
Conclusion. Vitamin D deficiency was associated with increased CIMT in female RA patients. Our finding suggests that hypovitaminosis D can be a risk factor for atherosclerosis in RA patients.

25OH Vitamin D was measured with one of the DIAsource 25OH Vitamin D RIA assay (KIP1961 or KIP1971).

- CANO F.J. (2014)

Longitudinal FGF23 and Klotho axis characterization in children treated with chronic peritoneal dialysis.
Clin. Kidney J., 7:457–463

Background. Fibroblast Growth Factor-23 (FGF23) and cofactor Klotho are key regulators of mineral metabolism in chronic kidney disease (CKD), but little is known about the mechanisms that regulate their production. This study evaluates longitudinal changes of FGF23 and Klotho levels and their regulatory factors in children on chronic peritoneal dialysis (PD).
Methods. FGF23, Klotho, 25(OH) vitamin D, 1,25-dihydroxyvitamin D and parathyroid hormone (PTH) plasma concentrations were measured during 1 year of follow-up in PD children. Anthropometric and dialytical parameters were evaluated in addition to mineral metabolism variables.
Results. Thirty-one patients under chronic PD were followed for 12 months. FGF23 mean plasma levels at Month 1 were significantly increased compared with controls, 215.1 ± 303.6 versus 9.4 ± 5.7 pg/mL, respectively (P < 0.001). Baseline Klotho levels were 41% lower in patients compared with controls, 132.1 ± 58 versus 320 ± 119.4 pg/mL, respectively (P < 0.001), and did not correlate with FGF23 and phosphorus levels. At Month 12, FGF23 (195 ± 300 pg/mL) and Klotho levels (130 ± 34 pg/mL) remained similar to baseline values. Log-FGF23 correlated significantly with height/age Z score (r = −0.38) and residual renal function (r = −0.44), but no correlation was found with serum phosphorus, phosphate intake, PTH and vitamin D levels. The log-FGF23 strongly correlated with calcium levels at Months 1, 6 and 12, however, this relationship was blunted if serum phosphorus was >6 mg/dL. By multiple regression analysis, calcium was the strongest variable determining FGF23 levels.
Conclusions. In this longitudinal study, FGF23 levels are markedly increased, and Klotho levels are reduced in PD children compared with controls. FGF23 levels appeared to be regulated primarily by serum calcium, showing a significant correlation at each time of measurement. This relationship was lost in patients with phosphorus >6 mg/dL. These observations may have important consequences to the therapeutic management of phosphate homeostasis in CKD patients.

$1,25(OH)_2$ Vitamin D was measured with the DIAsource $1,25(OH)_2$ Vitamin D RIA assay (KIP1929).

- CHOI K.M. (2014)

Impact of Visceral Fat on Skeletal Muscle Mass and Vice Versa in a Prospective Cohort Study: The Korean Sarcopenic Obesity Study (KSOS).

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PLoS ONE 9(12):e115407

Objectives: Sarcopenia and visceral obesity have been suggested to aggravate each other, resulting in a vicious cycle. However, evidence based on prospective study is very limited. Our purpose was to investigate whether visceral fat promotes a decrease in skeletal muscle mass and vice versa.
Methods: We observed changes in anthropometric and body composition data during a follow-up period of 27.6±2.8 months in 379 Korean men and women (mean age 51.9±14.6 years) from the Korean Sarcopenic Obesity Study (KSOS). Appendicular lean soft tissue (ALST) mass was calculated using dual-energy X-ray absorptiometry, and visceral fat area (VFA) was measured using computed tomography at baseline and follow-up examination.
Results: ALST mass significantly decreased, whereas trunk and total fat mass increased in both men and women despite no significant change in weight and body mass index. In particular, women with visceral obesity at baseline had a greater decrease in ALST mass than those without visceral obesity (P = 0.001). In multiple linear regression analysis, baseline VFA was an independent negative predictor of the changes in ALST after adjusting for confounding factors including age, gender, life style and body composition parameters, insulin resistance, high sensitivity C-reactive protein and vitamin D levels (P = 0.001), whereas the association between baseline ALST mass and changes in VFA was not statistically significant (P = 0.555).
Conclusions: This longitudinal study showed that visceral obesity was associated with future loss of skeletal muscle mass in Korean adults. These results may provide novel insight into sarcopenic obesity in an aging society.

25OH Vitamin D was measured with one of the DIAsource 25OH Vitamin D RIA assay (KIP1961 or KIP1971).

- TABATABAEI F. (2014)

Prevalence of vitamin D deficiency in healthy children in Kashan.
Proceeding of the 26th International Congress of Pediatrics – Oct 2014, Endocrine& Metabolic Disorders Abstracts: S9

Background: The data on the prevalence of vitamin D deficiency in healthy children from Iran is limited. Therefore, the current study was performed to evaluate the level of vitamin D in healthy children in Kashan.
Methods: The cases was selected from the healthy children aged 1-6 years who referred to the health centers for checking their weight and height during 2013. The children who were suffering from liver, kidney or any endocrine diseases or were on supplementary diet for vitamin D were excluded from the study. Prior to the start of the protocol, 3 cc of venous blood was drawn from the children. Standard DIA source kit and ELISA method were used to measure the level of 25-hydroxi vitamin D. Based on the criterion set results of the recent studies, the levels of vitamin D below the 10 nanograms per milliliter is classified as severely low, between 10 to 30 as low, 30 to 100 as normal and above 100 is defined as the toxic level.
Findings: In total, 100 children (54 boys, 46 girls) with mean age of 2.6 years were enrolled. The percentages of children with severely low, low, normal and toxic levels of 25(OH) D were 32, 47, 21 and 0, respectively.
Conclusion: Level of vitamin D was remarkably low in the children in this study. Nevertheless, further studies are recommended in this regard.

25OH Vitamin D was measured with the DIAsource 25OH Vitamin D Total ELISA assay (KAP1971).

- SCHWARTZ J.B. (2014)

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A comparison of direct and calculated free 25(OH) Vitamin D levels in clinical populations.
J. Clin. Endocrinol. Metab., 99(5):1631-7.

Calculated free 25 (OH) D levels varied considerably from direct measurements of free 25 (OH) D with discrepancies greatest in data for African Americans. Differences in DBP binding affinity likely contributed to estimation errors between the races. Directly measured free 25-OHconcentrations were related to iPTH but calculated estimates were not. Current algorithms to calculate free 25-OH vitamin D may not be accurate. Further evaluation of directly measured free 25 (OH) D levels to determine its role in research and clinical management of patients is needed.

Free 25OH Vitamin D was measured with the Future Diagnostics Free 25OH Vitamin D ELISA assay which is exclusively distributed by DIAsource (KARF1991).

- DEMKOW U. (2015)

Markers of Bone Metabolism in Children with Nephrotic Syndrome Treated with Corticosteroids.
Advs Exp. Medicine, Biology – Neuroscience and Respiration, 9:21-28

The aim of the study was to assess bone mineral density, bone metabolism markers, and vitamin D level in children with idiopathic nephrotic syndrome in the course of 1-year observation. Twenty five children with nephrotic syndrome aged 5-17 years were enrolled into the study. The median number of relapses was 6 (range 1-22). All patients were treated with prednisone and vitamin D (800 IU/day). Bone mineral density of total body (TB-BMD) and lumbar spine (L-BMD), evaluated by dual energy X-ray absorptiometry (DXA) expressed as Z-score, and serum calcium, phosphorus, parathormone (iPTH), alkaline phosphatase (ALP), bone alkaline phosphatase (BAP), osteocalcin (OC), albumin, creatinine, 25(OH)D3, 1,25(OH)2D3 and urine calcium/creatinine ratio (uCa/Cr) were evaluated at the enrollment visit and after 1 year of therapy. After 1 year significant decreases of TB-BMD Z-score (from -0.24 ± 1.34 to -0.74 ± 1.31, $p < 0.05$) and 25(OH)D3 serum level (from 31.7 ± 16.3 to 23.7 ± 9.3; $p < 0.05$) were observed. No other appreciable differences were found. At the study onset, negative correlations were found between L-BMD Z-score and serum ALP, BAP, and phosphorus and between TB-BMD Z-score and urine uCa/Cr. After 1 year, L-BMD Z-score correlated negatively with serum BAP and OC, and positively with serum 25(OH)D3. Multivariate analysis showed that BAP was the strongest predictor of L-BMD Z-score (beta = -0.49; $p < 0.05$). We conclude that children with nephrotic syndrome treated with corticosteroids are at risk of bone mass loss. Serum BAP concentration seems to be a good indicator of spongy bone metabolism in these children, who should be supplemented with vitamin D in an adjustable dose, possibly higher than 800 IU/24 h to prevent osteopenia.

1,25$(OH)_2$ Vitamin D was measured with the BioSource (now DIAsource) 1,25$(OH)_2$ Vitamin D RIA assay (KIP1929).

- RHEE Y. (2015)

Increased Sclerostin Levels after Further Ablation of Remnant Estrogen by Aromatase Inhibitors.
Endocrinol. Metab., 30(1):58-64

Background: Sclerostin is a secreted Wnt inhibitor produced almost exclusively by osteocytes, which inhibits bone formation. Aromatase inhibitors (AIs), which reduce the conversion of steroids to estrogen, are used to treat endocrine-responsive breast cancer. As AIs lower estrogen levels, they increase bone turnover and lower bone mass. We analyzed changes in serum sclerostin levels in Korean women with breast cancer who were treated with an AI.

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Methods: We included postmenopausal women with endocrine-responsive breast cancer (n=90; mean age, 57.7 years) treated with an AI, and compared them to healthy premenopausal women (n=36; mean age, 28.0 years). The subjects were randomly assigned to take either 5 mg alendronate with 0.5 µg calcitriol (n=46), or placebo (n=44) for 6 months.
Results: Postmenopausal women with breast cancer had significantly higher sclerostin levels compared to those in premenopausal women (27.8±13.6 pmol/L vs. 23.1±4.8 pmol/L, P<0.05). Baseline sclerostin levels positively correlated with either lumbar spine or total hip bone mineral density only in postmenopausal women (r=0.218 and r=0.233; P<0.05, respectively). Serum sclerostin levels increased by 39.9%±10.2% 6 months after AI use in postmenopausal women; however, no difference was observed between the alendronate and placebo groups (39.9%±10.2% vs. 55.9%±9.13%, P>0.05).
Conclusion: Serum sclerostin levels increased with absolute deficiency of residual estrogens in postmenopausal women with endocrine-responsive breast cancer who underwent AI therapy with concurrent bone loss.

25OH Vitamin D was measured with the BioSource (now DIAsource) 25OH Vitamin D3 RIA assay (KIP1961).

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Ordering Information

Description	Article code	Format
25OH Vitamin D Total ELISA	KAP1971	ELISA
25OH Vitamin D Total RIA	KIP1971	RIA
25OH Vitamin D3 RIA	KIP1961	RIA
Rat 25OH Vitamin D Total ELISA (RUO)	KRR1971	ELISA
Free 25OH Vitamin D ELISA (RUO)	KARF1991	ELISA
$1,25(OH)_2$ Vitamin D ELISA	KAP1921	ELISA
$1,25(OH)_2$ Vitamin D RIA	KIP1929	RIA

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