Vitamin D and Cancer studies:


**Diagnosis and treatment of vitamin D deficiency.**

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The recent discovery - in a randomised, controlled trial - that daily ingestion of 1100 IU of colecalciferol (vitamin D) over a 4-year period dramatically reduced the incidence of non-skin cancers makes it difficult to overstate the potential medical, social and economic implications of treating vitamin D deficiency. Not only are such deficiencies common, probably the rule, vitamin D deficiency stands implicated in a host of diseases other than cancer. The metabolic product of vitamin D is a potent, pleiotropic, repair and maintenance, secosteroid hormone that targets > 200 human genes in a wide variety of tissues, meaning it has as many mechanisms of action as genes it targets. A common misconception is that government agencies designed present intake recommendations to prevent or treat vitamin D deficiency. They did not. Instead, they are guidelines to prevent particular metabolic bone diseases. Official recommendations were never designed and are not effective in preventing or treating vitamin D deficiency and in no way limit the freedom of the physician - or responsibility - to do so. At this time, assessing serum 25-hydroxy-vitamin D is the only way to make the diagnosis and to assure that treatment is adequate and safe. The authors believe that treatment should be sufficient to maintain levels found in humans living naturally in a sun-rich environment, that is, > 40 ng/ml, year around. Three treatment modalities exist: sunlight, artificial ultraviolet B radiation or supplementation. All treatment modalities have their potential risks and benefits. Benefits of all treatment modalities outweigh potential risks and greatly outweigh the risk of no treatment. As a prolonged 'vitamin D winter', centred on the winter solstice, occurs at many temperate latitudes, <= 5000 IU (125 mug) of vitamin D/day may be required in obese, aged and/or dark-skinned patients to maintain adequate levels during the winter, a dose that makes many physicians uncomfortable.

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Seasonal and geographical variations in lung cancer prognosis in Norway. Does Vitamin D from the sun play a role?

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Vitamin D derivatives can modulate proliferation and differentiation of cancer cells. Our main source of Vitamin D is ultraviolet (UV) radiation-induced synthesis in skin following sun exposure. UV measurements show that the ambient annual UV exposures increase by about 50% from north to south in Norway. As judged from the incidence rates of squamous cell carcinoma, the same is true for the average personal UV exposures. Solar ultraviolet B (UVB) (280-320nm) exhibits a strong seasonal variation with a minimum during the winter months. The present work aims at investigating the impact of season of diagnosis and residential region, both influencing the Vitamin D level, on the risk of death from lung cancer in patients diagnosed in Norway. Data on all incident cases of lung cancer between 1964 and 2000 were collected. Risk estimates were calculated as relative risk (RR), with 95% confidence intervals using Cox regression model. The seasonal variation of 25-hydroxyvitamin D was assessed from routine measurements of 15,616 samples performed at The Hormone Laboratory of Aker University Hospital. Our results indicate that season of diagnosis is of prognostic value for lung cancer patients, with a approximately 15% lower case fatality for young male patients diagnosed during autumn versus winter (RR=0.85; 95% CI, -0.73 to 0.99; p=0.04). Residing in a high UV region resulted in a further lowering of the death risk than residing in a low UV region. We propose, in agreement with earlier findings for prostate-, breast- colon cancer and Hodgkins lymphoma, that a high level of sun-induced 25-hydroxyvitamin D can be a prognostic advantage for certain groups of lung cancer patients, notably for young men. Lung cancer has for several decades been the leading cause of cancer-related mortality in men in Norway and during the last two decades, became the second most common cause of cancer-related death in women. There are two main types of lung cancer: small cell lung cancer for which chemotherapy is the primary treatment and non-small cell lung cancer, which in its early stages is treated primarily with surgery. Gender-related differences have been described in the literature with respect to survival after therapy, male gender being a significant independent negative prognostic factor. In Norway the 5 years relative survival for localized tumours is about 30% for females and 20% for males. Calcitriol, which is the most active form of Vitamin D, is involved in key
regulatory processes such as proliferation, differentiation and apoptosis in a wide variety of cells. Mechanisms for these actions have been proposed to be the interaction of active Vitamin D derivatives with a specific nuclear receptor (VDR receptor) and/or with membrane targets. In vitro studies, performed with lung cancer cell lines, have shown an inhibitive effect of Vitamin D derivatives on cell-growth and proliferation. Furthermore, animal studies have demonstrated the capability of these compounds to suppress invasion, metastasis and angiogenesis in vivo, suggesting that administration of Vitamin D derivatives may be used as adjuvant therapy for lung cancer. Humans get optimal Vitamin D levels by exposure to sun or artificial ultraviolet B (UVB, 280-320nm) sources, and possibly also by consumption of food rich in this nutrient (fat fish, eggs, margarine, etc.) or of vitamin supplements. Among these sources, solar radiation appears to be the most important one. Thus, the Vitamin D status (assessed by the serum levels of 25-hydroxyvitamin D, calcidiol) exhibits a strong seasonal variation that parallels the seasonal change in the fluence of solar UVB that reaches the ground. During winter, the UVB fluence rate in the Nordic countries (50-71 degrees N) is below the level required for Vitamin D synthesis in skin. The maximal level of calcidiol is reached between the months July and September, and is 20-120% higher than the corresponding winter level. Recently we hypothesised that the seasonal variation of calcidiol might be of prognostic significance for colon-, breast- prostate cancer as well as for Hodgkins lymphoma in Norway. Patients diagnosed during summer and autumn have a better survival after standard treatment than patients diagnosed during the winter season. This might be a consequence of a higher Vitamin D level. An American study investigated the effect of season of surgery and recent Vitamin D intake on the survival of non-small cell lung cancer patients. The authors reported a significant beneficial joint effect of summer season and high Vitamin D intake compared with winter season and low Vitamin D intake while Vitamin D intake alone did not affect prognosis. Similar results were recently reported from a large study in United Kingdom involving over a million cancer patients including over 190,000 patients diagnosed with lung cancer. Norway (58-71 degrees N) has a significant north-south variation in UV fluence. This makes the country suitable for studies relating cancer epidemiology to UV levels. We investigated whether variations in UV, and, consequently, in Vitamin D level, influence the prognosis of lung cancer, using season of diagnosis and residential regions as variables. Survival data obtained for patients diagnosed over a 40 years period were compared with variations in serum Vitamin D levels obtained from routine measurements performed in The Hormone Laboratory of Aker University Hospital during the period 1996-2001. Seasonal and gender variations in Vitamin D level have been estimated from the analyses.