antibodies in autoimmune hepatitis, type 1.[3–5] In relation to therapy, patients with minocycline hepatitis without jaundice can usually be managed by simple withdrawal of the drug. In contrast, patients with severe hepatitis often require treatment with corticosteroids but only for a limited period of 2–4 months. This differs from the recommendation of immunosuppressive therapy for at least 2 years in patients with autoimmune hepatitis, type 1.

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References

1 Elkayam O, Yaron M, Caspi D. Minocycline-induced autoimmune syndromes: an overview. *Semin Arthritis Rheum* 1999; **28**: 392–7.
2 Lawrenson RA, Seaman HE, Sundström A, Williams TJ, Farmer RDT. Liver damage associated with minocycline use in acne. *Drug Safety* 2000; **23**: 333–49.
3 Krawitt EL. Autoimmune hepatitis. *N Engl J Med* 2006; **354**: 54–66.
4 Teitelbaum JE, Perez-Atayde AR, Cohen M, Bousvaros A, Jonas MM. Minocycline-related autoimmune hepatitis. *Arch Pediatr Adolesc Med* 1998; **152**: 1132–6.
5 Goldstein NS, Bayati N, Silverman AL, Gordon SC. Minocycline as a cause of drug-induced autoimmune hepatitis. *Am J Clin Pathol* 2000; **114**: 591–8.

General Correspondence

Sufficient knowledge of the health benefits of vitamin D exists to modify public health recommendations now

The recent editorial on vitamin D and prevention of chronic disease[1] took an inappropriately pessimistic position, as did a review by a working group of the International Agency for Cancer Research.[2] There is mounting evidence that vitamin D significantly reduces the risk of cancer and other chronic diseases as well as many infectious diseases.

Much of the understanding of the role of solar ultraviolet-B (UVB) and vitamin D is based on ecological studies. Contrary to what was stated in the editorial, confounding factors have been incorporated into several studies. In an ecological study of cancer mortality rates in the United States, indices for the following cancer risk-modifying factors were used: summertime solar UVB, smoking, alcohol consumption, ethnic heritage, urban/rural residence and socioeconomic status;[3] the results for the non-UVB factors were in very-good-to-excellent agreement with the literature, and solar UVB was found inversely correlated with 15 types of cancer. In subsequent studies, additional factors were added including those for air pollution, diet, and wintertime solar UVB, and are discussed in a recent paper.[4] As a result of such studies, 17 types of cancer have been found inversely correlated with solar UVB doses. There are several important reasons why ecological studies of cancer rates in the United States are to be considered reliable: solar UVB doses in summer in the western states are much higher than those in the eastern states at the same latitude because of higher surface elevations and thinner stratospheric ozone layer, an asymmetry that permits distinction from risk factors varying simply with latitude; solar UVB doses in summer are sufficiently high to generate 1000–2000 IU/day of vitamin D from casual irradiance in the southwestern states; and reliable indices can be found for many important cancer risk-modifying factors.

There is also excellent additional information on the role of vitamin D in reducing the risk of cancer from observational studies and a randomized controlled trial. A meta-analysis of observational studies found that there is a 50% reduction in colorectal cancer incidence rate for a serum 25-hydroxyvitamin D [25(OH)D] level of 34 ng/mL compared with 6 ng/mL.[5] A randomized controlled trial of calcium and vitamin D supplementation involving post-menopausal women living in Nebraska found a 77% reduction in all-cancer incidence between the ends of the first and fourth years for those taking 1450 mg/day of calcium and 1100 IU/day of vitamin D, of which 40% was attributed to calcium and 35% to vitamin D.[6] A recent review concluded that solar UVB and vitamin D reduce the risk of cancer in a manner that satisfies Koch's postulates as outlined by Hill.[7]

It is possible to estimate the reduction in mortality rates for various diseases if the mean serum 25(OH)D level for Australians, currently estimated at 25 ng/mL,[8] were raised to 40 ng/mL. The estimated reductions range from 10% for dementia and chronic lower respiratory diseases, 20% for diabetes, 25% for stroke, 30% for ischaemic heart disease, heart failure, and influenza, and 35% for cancer.[9] From data on deaths by disease for 2006 from the Australian Bureau of Statistics,[10,11] it is estimated that the death rate could be reduced by 26 500/year. By

comparison, 1648 Australians died from melanoma or non-melanoma skin cancer in 2006.[10]

Additional research to evaluate the role of solar UVB and vitamin D in reducing the risk of chronic and infectious diseases would certainly be welcomed. However, in my opinion, sufficient information already exists to recommend serum 25(OH)D levels > 40 ng/mL as such levels have been demonstrated to greatly reduce the risk of many types of disease. While the concern about melanoma and skin cancer is real for Australians because those of Northern European ancestry do not have skin pigmentation adapted for the high solar UV doses present, there should be ways to increase serum 25(OH)D levels without increasing skin cancer rates, perhaps by making sure that UVA (320–400 nm) irradiance is reduced with better sunscreens to lower the risk of melanoma and suggesting short solar UV irradiances near solar noon with as much skin exposed as possible.

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References

1 Neale RE, Webb PM, van der Pols JC. Vitamin D for prevention of chronic disease: the need for continued research. *Intern Med J* 2008; **38**: 813–15.
2 *IARC Working Group Report 5: Vitamin D and Cancer* (25 November 2008) [cited 2009 Feb 2]. Available from: URL: http://www.iarc.fr/en/Media-Centre/IARC-News/Vitamin-d-and-cancer
3 Grant WB, Garland CF. The association of solar ultraviolet B (UVB) with reducing risk of cancer: multifactorial ecologic analysis of geographic variation in age-adjusted cancer mortality rates. *Anticancer Res* 2006; **26**: 2687–99.
4 Grant WB. A critical review of Vitamin D and cancer: a report of the IARC Working Group on vitamin D. *Dermato-Endocrinology* 2009; **1**: 22–30.
5 Gorham ED, Garland CF, Garland FC, Grant WB, Mohr SB, Lipkin M *et al.* Optimal vitamin D status for colorectal cancer prevention a quantitative meta analysis. *Am J Prev Med* 2007; **32**: 210–16.
6 Lappe JM, Travers-Gustafson D, Davies KM, Recker RR, Heaney RP. Vitamin D and calcium supplementation reduces cancer risk: results of a randomized trial. *Am J Clin Nutr* 2007; **85**: 1586–91.
7 Grant WB. How strong is the evidence that solar ultraviolet B and vitamin D reduce the risk of cancer? An examination using Hill's criteria for causality. *Dermato-Endocrinology* 2009; **1**: 14–21.
8 van der Mei IA, Ponsonby AL, Engelsen O, Pasco JA, McGrath JJ, Eyles DW *et al.* The high prevalence of vitamin D insufficiency across Australian populations is only partly explained by season and latitude. *Environ Health Perspect* 2007; **115**: 1132–9.
9 Grant WB, Cross HS, Garland CF, Gorham ED, Moan J, Peterlik M *et al.* Estimated benefit of increased vitamin D in reducing economic burden of disease in Europe. *Prog Biophys Mol Biol*. 2009 Mar 4 [Epub ahead of print].
10 Australian Bureau of Statistics. *Causes of Death, Australia*, 2006; (cat no. 3303.0) [cited 2009 Jan 12]. Available from: URL: http://www.abs.gov.au/AUSSTATS/abs@.nsf/ProductsbyTopic/2093DA6935DB138FCA2568A9001393C9?OpenDocument
11 Australian Bureau of Statistics. *Cancer in Australia A Snapshot, 2004-05*. (cat no. 4822.0.55.001) 2006 [cited 2009 Jan 12]. Available from: URL: http://www.abs.gov.au/AUSSTATS/abs@.nsf/ProductsbyTopic/8DDD5AED085834DACA256F010077BE4A?OpenDocument

Reply

We thank Dr Grant for his response to our Editorial.

Grant believes that there is sufficient evidence for a protective effect of vitamin D on mortality from a number of conditions and appears to recommend that Australians should increase their sun exposure to increase their serum levels of vitamin D.[1] We believe that this is an unfounded and potentially dangerous proposition.

Our concerns, and those of an expert committee convened by the International Agency for Research on Cancer,[2] are that although suggestive, the current evidence for a protective effect of vitamin D is far from conclusive. Ecological studies, even those that take possible confounding factors into account, are useful for generating hypotheses, but they cannot be used to infer causality because neither the exposure of interest nor the confounding factors are measured at an individual level.[3] While a meta-analysis of observational studies (case–control and cohort studies) concluded that higher serum levels of vitamin D are associated with a significantly reduced risk of colon cancer and a non-significantly reduced risk of breast cancer,[2] it is difficult to establish from these study types whether low vitamin D status is a causal factor for cancer or simply a marker of poorer health status. The known associations between low serum vitamin D and other markers of poor health status, such as high body mass index, low physical activity and