

A review of the role of solar ultraviolet-B irradiance and vitamin D in reducing risk of dental caries

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Large geographical variations in dental health and tooth loss among US adolescents and young adults have been reported since the mid-1800s. Studies in the 1920s and 1930s noted that vitamin D and ultraviolet-B (UVB) irradiance reduced caries formation, the proposed mechanism being improved calcium absorption and metabolism. This paper reviews the history of studies of dental caries with respect to vitamin D, geographical location and available solar UVB doses. In addition, data on mean dental health rank by state for US servicemen from three periods, 1918, 1934 and 1943, were used in regression analyses with respect to summertime solar UVB doses and an index for mottled enamel, a proxy for natural fluoridation of drinking water, for 1935. There was a significant inverse correlation for dental health rank with respect to solar UVB from doses of 4.0 to 6.5 kJ/m² with little change thereafter. Adding data for mottled enamel rates for the states with UVB doses <6.6 kJ/m² improved the adjusted R² from 0.45 to 0.52. The mechanism whereby UVB reduces risk of dental caries is likely through production of vitamin D, followed by induction of cathelicidin and defensins, which have antimicrobial properties. Serum 25-hydroxyvitamin D concentrations at or above 30–40 ng/ml should significantly reduce the formation of dental caries. It is unfortunate that the UVB and vitamin D findings were not given more consideration in the 1950s as a way to reduce the risk of dental caries when water fluoridation was being proposed.

Introduction

Dental caries is one of the most prevalent diseases in humans. It is the primary source of tooth loss for those younger than 40 years, with periodontal disease being the primary cause after that age.¹ Loss of homeostasis of an oral cavity overgrown with *Streptococcus mutans* are the primary cause of the disease.² *S. mutans* adheres strongly and releases acids by the fermentation of carbohydrates, thereby demineralizing the tooth.³ Eating sweets and not brushing teeth both contribute to the formation of dental caries,⁴ but less well known is that solar ultraviolet-B (UVB)

irradiance, through additional production of vitamin D and vitamin D supplementation in deficiency appears to reduce the risk of caries.

This study reviews the literature on UVB, vitamin D and dental caries (as identified using the search terms 'vitamin D, dental caries, ultraviolet' in PubMed and www.scholar.google.com). It also includes an ecological analysis of dental condition by state, for men in the US armed forces during World War I and II and Navy servicemen in between those wars⁵ versus July solar UVB doses.

Results

A moderate-sized body of literature exists on the role of geographic location and solar UVB in association with reduced risk of dental caries in the United States and Australia. The first study finding a latitudinal gradient in dental caries was a report of men rejected from the draft for the Civil War for lost teeth, from 8 per 1,000 men in Kentucky to 25 in New England.⁶ However, no reason seems to have been given to explain the finding.

There were several studies reported on vitamin D and dental caries in the 1920s and 1930s. May Mellanby and coworkers in Sheffield, England, did studies on the role of vitamin D on teeth in the 1920s. The first experiments were with dogs, where it was found that vitamin D stimulated the calcification of teeth.⁷ Subsequently, they studied the effect of vitamin D on dental caries in children, finding a beneficial effect.⁷ Additional studies were conducted on children in New York regarding dental caries with respect to season, artificial UVB irradiance and oral intake of vitamin D with the finding that it took 800 IU/d to prevent caries effectively.⁸

Using data for adolescent males aged between 12 and 14 years from a cross-sectional survey in 1933–1934,⁹ Mills¹⁰ first linked the geographical variation in prevalence to sunlight exposure. He placed isopleths of arithmetic averages of county indices of dental caries incidence for schoolchildren living in rural areas or towns with populations of less than 5,000 in 19 states on a map of the United States. This mapping showed a general increase with increasing latitude, with an anomaly in the Rocky Mountain States. A factor of greater than three existed between the indices for Oklahoma and Pennsylvania (150 and 531 caries/100 children, respectively); there was also an inverse correlation with respect to

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water hardness, regression analysis showing a reduction of 33% for >500 ppm versus <50 ppm total mineral levels, with calcium and magnesium important components. Using the same data set, East¹¹ found that dental caries were inversely related to mean hours of sunlight/year, with those living in the sunny west (3,000 hours of sunlight/year) having half as many carious lesions as those in the much less sunny northeast (<2,200 hours of sunlight/year); rates in areas with intermediate annual hours of sunlight fell between those for the extremes of sun exposure. East referred to other contemporaneous papers indicating a role of vitamin D⁸ and season¹² in affecting the risk of caries. Many other studies reported geographical variations in dental caries, sometimes linking the variations to differences in solar radiation. If a mechanism for the effect of sunlight was proposed, it was production of vitamin D and improved calcium absorption and metabolism.

Several studies were conducted in Oregon in the 1950s. It was noted that dental caries prevalence was lower in the sunnier parts of the state, a finding that persisted after considering other factors that affect dental caries rates.¹³⁻¹⁵ The mechanism was attributed to vitamin D through its effects on calcium metabolism.

Table 1 summarizes the results from previous studies.

A study of dental health rank, by state of origin, for United States draftees to World War I, Navy servicemen in 1934, and Army servicemen in 1943 was reported by Dunning.⁵ Ranking was based on decayed and missing teeth as well as filled teeth for the Navy veterans. These were averaged ranks for each of the 48 states and ranged from 2 (Arkansas) to 45 (Rhode Island). The highest ranks were near Texas and the lowest in the Northeast. These dental health rank scores were plotted versus July UVB doses and the index of mottled enamel from 1936.²⁵ **Figure 1** gives the dental health score ranks by state for men entering the armed forces during World War I and II¹⁵ versus July solar UVB dose. Dental health decreased in a nearly linear fashion as UVB dose increased up to UVB levels of 6.5 kJ/m², above which there was little additional change. The regression relationship for UVB below 6.5 kJ/m² for rank is 87-12x UVB dose ($r = -0.68$, adjusted $r = 0.45$ $p < 0.001$) and above 7 kJ/m² is 20-0.69x UVB dose ($r = 0.07$). This finding is similar to previous observations for many types of cancer.^{26,27} In a regression analysis restricted to those states with UVB doses <6.6 kJ/m, with inclusion of the mottled enamel index, the association was increased, giving a normalized correlation coefficient, β , of -0.63, $p < 0.001$ for UVB and of -0.30, 0.03 for mottled enamel; the adjusted R^2 being increased to 0.52.

Figure 2 shows a plot of July solar UVB doses (http://toms.gsfc.nasa.gov/ery_uv/dna_exp.gif) and 1935 mottled enamel indices²⁵ versus dental health rank. States with dental health 30 or greater had a mean UVB dose of 4.5 kJ/m². While the linear fit for each data set sloped downwards with increased rank, the correlation coefficient, r , was -0.71, $p \leq 0.001$ for UVB and -0.37, $p = 0.01$ for fluorosis. In a multiple linear regression analysis, the addition of fluorosis to UVB did not change the result.

Discussion

These results indicate that from the mid-1800s through the 1980s, solar UVB was inversely correlated with dental caries and

tooth loss among adolescents and young men. Tooth loss and dental caries rates between low- and high-UVB-dose states in the mid-1800s and 1933 differed by factors of three. In both periods, little to no understanding existed of the role of UVB or vitamin D in reducing risk of dental caries.

Although the original mechanism proposed for UVB and vitamin D related to calcium metabolism,⁷ the effect is at least as likely to involve vitamin D and its induction of the antimicrobials cathelicidin and defensins as already noted to be important in periodontitis.²⁸ In recent years several papers have discussed how cathelicidin and defensins reduce the risk of dental caries through attacking oral bacteria linked to dental caries.²⁹⁻³⁵ However, these papers apparently did not discuss the involvement of vitamin D in the process. These polypeptides reduce the risk of several other types of bacterial infections, such as tuberculosis,³⁶ pneumonia,^{37,38} and severe sepsis.³⁹⁻⁴¹ In 1928, Mellanby⁷ stated *"It is interesting to note that even in sections of teeth in which caries appears to be completely arrested the dentinal tubules may contain micro-organisms. These, however, are apparently inactive."*

Low serum 25(OH)D status has also been reported as a risk factor for periodontal disease, reviewed in Grant and Boucher.⁴² One recent paper found vitamin D insufficiency (serum 25(OH)D <30 ng/mL) is associated with maternal periodontal disease during pregnancy.⁴³

The serum 25(OH)D 'level' necessary for dental caries reduction does not appear to have been worked out in detail, but it might be inferred from studies of other diseases. Serum 25(OH)D level-cancer incidence relations for breast and colorectal cancer start to flatten around 30–40 ng/mL.⁴⁴ This value is in accord with a recent observational study on incidence of influenza, which found 38 ng/mL to be the lower end of the optimal range.⁴⁵ Vitamin D confers many health benefits, including reduced risk of cancer and infectious diseases, as mentioned earlier, as well, it is suggested, of cardiovascular disease and type 2 diabetes mellitus,⁴⁶ autoimmune diseases, falls, fragility fractures and many other diseases⁴⁷ and may improve physical fitness⁴⁸ and age-adjusted brain function.⁴⁹ It was estimated that if all Americans could raise their serum 25(OH)D levels to more than 40 ng/mL, all-cause mortality rates could be predicted to decrease by about 15%.⁵⁰ Similar effects have been estimated for other countries including Canada⁵¹ and Nordic countries.⁵² A recent review both underscored the global importance of vitamin D and proposed changes to vitamin D nutritional policies.⁵³ Thus, serum levels above 30–40 ng/mL may significantly reduce the risk of dental caries, but more research is required to determine the serum 25(OH)D level-caries risk relationship.

Casual solar UVB irradiance in summer can raise serum 25(OH)D levels by 10–15 ng/mL, on average, in those aged 45 years living in England.⁵⁴ Higher increases are likely for young people living in the United States. Vitamin D production from solar UVB depends on many factors, including age, skin pigmentation, body mass index, surface area exposed, time of day and geographic location but the easiest way to raise serum 25(OH)D levels is through vitamin D3 supplementation. For most people, increases of 10–15 ng/mL would require intakes of 1,000–2,000 IU/day.⁵⁵ However, there is considerable person-to-person

Table 1. Summary of findings in earlier studies of geographic variation of dental caries

| Location | Finding | Reference |
|----------------------------|--|-----------|
| Northeastern United States | A significant increase of men rejected from the draft for the Civil War for lost teeth, from 8 per 1,000 men in Kentucky to 25 in New England. | 6 |
| England | Children aged 5–9 years were given vitamin D ₂ and followed for 28 weeks. Those taking higher doses of vitamin D ₂ developed fewer caries than controls taking lower amounts or none. | 7 |
| United States | A general increase in dental caries for school boys aged 12–14 years, with lower rates in the Rocky Mountains; controlled for water hardness. | 10 |
| United States | Seasonal incidence of dental caries | 12 |
| New York | The role of vitamin D in dental caries | 8 |
| United States | The number of dental caries for boys aged 12–14 years varied by a factor of two from east to west with the number of hours of annual sunshine. | 11 |
| United States | Summarized previous data on dental caries among those called to the Armed Forces such as the Navy, showing latitudinal effect, although sunshine was not mentioned. Showed that a similar latitudinal effect for tooth loss was apparent in the northern states in 1963–64. | 16 |
| United States | Inverse correlation of dental caries with amount of available sunshine noted. | 17 |
| United States | Sunshine and production of vitamin D, thought vitamin D increased calcification during tooth formation. | 18 |
| Oregon | Fewer dental caries in school children living in sunny inland county compared to coastal county; controlled for fluoride in water supply, density of dentists, candy bars and carbonated drinks. | 13, 14 |
| United States | Dental disease rankings by state of draftees to World War I, 1918 [decayed, missing teeth (DMT)], Navy, 1934 [decayed, missing and filled teeth (DMFT)], and Army, 1943 (DMT). The lowest disease rate was in Texas and Alabama, the worst in Maine. For any longitude band, there was a significant increase in dental disease with increasing latitude. Correlated with hours of sunlight; also with consumption of baked goods (refined carbohydrates); also with relative humidity as well as rainfall, which could leach minerals from the soil | 5 |
| South Africa | Declining number of dental caries for children with increasing distance from the east coast; analysis restricted to magisterial districts with less than 0.7 ppm fluoride in the water. Sunshine noted to increase with distance from the east coast. | 5 |
| Oregon | Inverse correlation found for native white boys aged 14–16 years with respect to location and altitude, linked to amount of sunshine available. Checked for fluoride in drinking water, finding little use at that time. Also, for water selenium content a modest direct correlation was found. | 15 |
| Chile | Mean dental caries for 12–14 year old children in 1945 were 3.8, 7.1 and 8.8 for northern (18°–32°S), central (32°–40°S) and southern (40°–55°S) regions. Some of this effect was attributed to fluoride in the drinking water, but the data do not support this interpretation. | 19 |
| Eastern United States | Studied boys aged 12–14 years. Included towns with <0.3 ppm fluoride in drinking water. Inverse correlation with selenium in soil, but that did not explain all of the variance, with highest rates in New England, lowest in southern Atlantic states. | 20 |
| Australia | The variation of dental caries in members of the Royal Air Force was compared to latitude and multiple sclerosis (MS) death rate. Correlation coefficient with MS was 0.97 ($p < 0.002$). Risk of MS had been linked to high dietary fat and low vitamin D status. | 21 |
| United States | Data from Dunning. ⁵ Correlation coefficient with MS was 0.55 ($p < 0.001$) | 21 |
| World | Data for MS prevalence and dental caries for 45 countries. Correlation coefficient for dental caries with MS was 0.78 ($p < 0.001$). | 21 |
| Burma | DMF scores in children were measured for 12 towns. An inverse correlation with daily mean hours of bright sunshine was found ($b = -0.38$, $p < 0.01$) | 22 |
| Australia | DMF scores in 12-yr-old children were higher in the southern states, and rates of edentulousness in 35–44-yr-olds in Tasmania (latitude 40°–45°S) were double those for people in more northerly states. | 23 |
| U.K. | A study of 11-year-old children from across England and Wales, Scotland, Isle of Man, and Jersey was conducted in 2004/5. Mean D3MFT across England was 0.64 (D3T = 0.32, MT = 0.06, FT = 0.25), across Wales it was 1.09 (D3T = 0.48, MT 0.11, FT = 0.50), and across Scotland values were 1.29 (D3T = 0.52, MT = 0.17, FT = 0.60). | 24 |

variability in serum 25(OH)D with respect to oral intake,⁵⁶ so testing 25(OH)D levels is recommended for those wishing to achieve specific levels.

It is interesting that studies have found little difference in dental caries rates between African American and white American children.⁵⁷ Those of African descent have more calcium in their

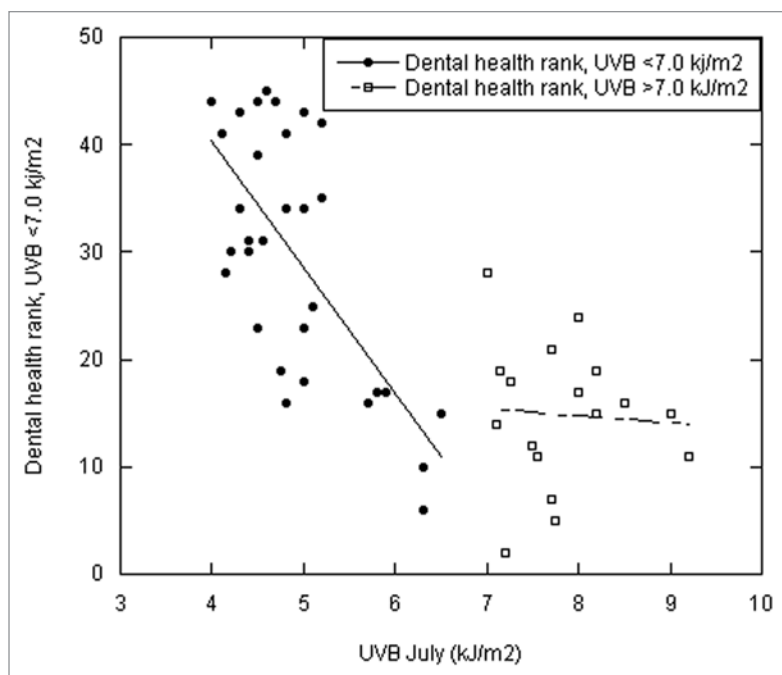


Figure 1. Dental health ranking, by state, for men entering the armed forces during World War I and II versus July solar UVB dose.

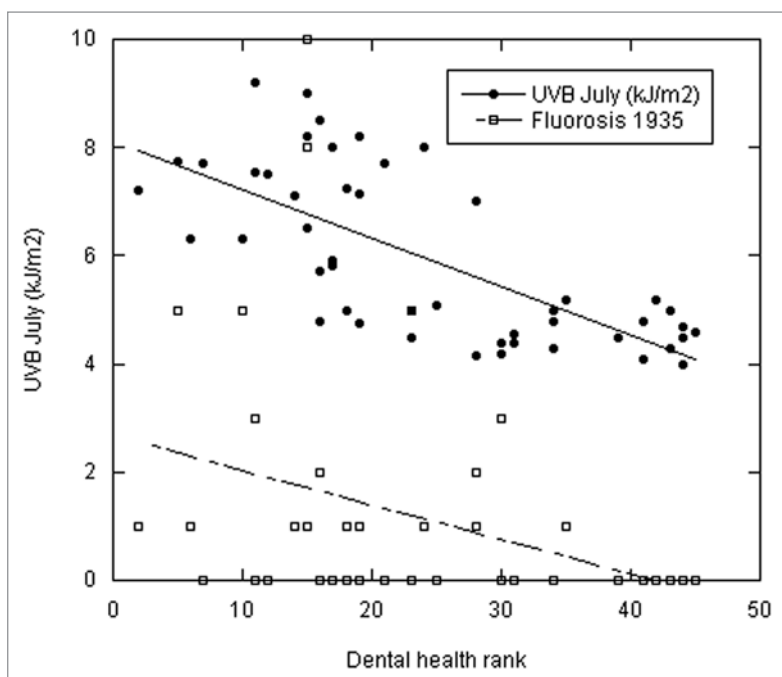


Figure 2. Plot of July solar UVB doses and mottled enamel index for 1935 vs. dental health rank by state for U.S. servicemen from 1918-1943.

bones than white people.⁵⁸ They are also likely to have more calcium in their teeth. These data may reflect genetic factors or, in immigrants, higher sun exposure in early life.

The finding of maximal dental health with UVB doses of about 6.5 kJ/m², is interesting though it is also possible, though

unlikely, that fluoride levels in drinking water are lower in the sunnier states, primarily in the southwest (See Fig. 2.).

Since the studies reviewed and the analyses presented are ecological studies and their are due to the usual limitations of such studies. One limitation here is lack of information on dietary factors such as sugar consumption rates, which are important risk factors for dental caries. This analysis assumed that dietary factors were the same for all regions. This assumption is more likely to be satisfied in a single-country study than in a multi-country study, but it still leads to some uncertainty. Another limitation is that the dental index developed by Dunning⁵ was not expressed as a quantitative measure of dental caries. Thus, the relation shown in **Figure 1** does not translate directly into a dose-response relation. Another limitation is that summertime solar UVB doses were used as the index of vitamin D production whilst vitamin D production and serum 25(OH)D levels are important during the entire year. Wintertime deficiency of vitamin D lasts several months in the higher-latitude States⁵⁹ but is much shorter in States at lower latitudes whilst skin pigmentation also plays a role in vitamin D production but could not be adjusted for.

Fluoridation of municipal drinking water is currently widespread in the United States. It was introduced in Grand Rapids, Michigan in 1945.^{60,61} Comparisons of dental caries in 1945 and 1949 in Grand Rapids, Muskegon (with low water fluoride content) and in Aurora, Illinois, with natural fluoridation (at 1.2 ppm) showed that by age 15 years, those in Aurora had one-third the number of dental caries as those in the two Michigan cities whilst for under 7 years old, the dental caries rates were nearly the same for Grand Rapids as for Aurora. Based on this experiment, fluoridation was widely adopted and spread to most states by the 1980s. However, that study was conducted in the Northeast, where solar UVB doses are much lower than in the Southwest. By the end of 1992, 10,567 public water systems serving 135 million persons in 8,573 US communities had instituted water fluoridation.⁶² While widely accepted as a primary reason for decreases in dental caries,⁶³ there is reason to doubt this claim. For example, dental caries have continued to decline in two European regions after water fluoridation was discontinued.^{64,65} Dental caries are considered primarily due to consumption of refined sugar and a low frequency of tooth brushing in Europe.⁴ In addition, adverse effects of excessive water fluoridation can be severe, including 'moderate dental fluorosis, stage I skeletal fluorosis (arthritis with joint pain and stiffness), decreased thyroid function and detrimental effects on the brain, especially in conjunction with aluminum.^{66,67} Many papers on the adverse health effects are published in the journal Fluoride (www.fluorideresearch.org). Furthermore, The US

Environmental Protection Agency recently announced proposed rules to limit fluoride level in drinking water to 0.7 milligrams of fluoride per liter of water due to risk of fluorosis for higher levels.⁶⁸

It is unfortunate that water fluoridation, rather than promotion of sunlight and vitamin D fortification of food and the use of supplements, was adopted as the public health approach to reducing dental caries in the United States and elsewhere, especially since better vitamin D status has many additional benefits.^{47,50} However, fluoridation of drinking water to 1 ppm entails an ~12.5% (95% CI, 7.0%–21.5%) risk of dental fluorosis, a fluoride-induced mottling of the enamel.⁶⁹ Thus topical application of fluoride, such as through the use of fluoridated toothpaste, seems to provide a useful alternative to drinking water fluoridation.⁷⁰

Methods

Data sources. Solar UVB data for July 1992 are from NASA Goddard (http://toms.gsfc.nasa.gov/ery_uv/dna_exp.gif) and were digitized by state and adjusted for population distribution producing a data set already used in several ecological studies of cancer.^{26,27}

Wintertime solar UVB availability is proportional to latitude and solar zenith angle. Previous work reports associations, best described by a quadratic function, between latitude and prevalence of multiple sclerosis in the United States.^{71–73} Because of apparent exceptions to a simple latitudinal gradient of dental condition in the United States, especially at latitudes below 40° N, the present report does not use latitude in any analyses.

References

1. Murray H, Locker D, Kay EJ. Patterns of and reasons for tooth extractions in general dental practice in Ontario, Canada. *Community Dent Oral Epidemiol* 1996; 24:196–200.
2. Parisotto TM, Steiner-Oliveira C, Silva CM, Rodrigues LK, Nobre-dos-Santos M. Early childhood caries and mutans streptococci: a systematic review. *Oral Health Prev Dent* 2010; 8:59–70.
3. Islam B, Khan SN, Khan AU. Dental caries: from infection to prevention. *Med Sci Monit* 2007; 13:196–203.
4. Zaborskis A, Milcivienė S, Narbutaitė J, Bendoraitienė E, Kavaliauskienė A. Caries experience and oral health behaviour among 11–13-year-olds: an ecological study of data from 27 European countries, Israel, Canada and USA. *Community Dent Health* 2010; 27:102–8.
5. Dunning JM. The influence of latitude and distance from seacoast on dental disease. *J Dent Res* 1953; 32:811–29.
6. Lewis JR. Exemptions from military service on account of loss of teeth. *Dental Cosmos* 1865; 7:240–2. (in East BR. Some epidemiological aspect of tooth decay. *Am J Pub Health* 1942; 32:1424–50).
7. Mellanby M, Pattison CL. The action of vitamin D in preventing the spread and promoting the arrest of caries in children. *Brit Med J* 1928; 2:1079–82.
8. McBeath EW, Zucker TF. The Role of vitamin D in the control of dental caries in children. *J Nutrition* 1938; 15:6.
9. US Pub Health Service. Dental Survey of School Children, Ages 6–14 Years Made in 1933–4 in 268 States. *Pub. Health Bull.* %226, US Pub Health Service, Washington DC May 1936.
10. Mills CA. Factors Affecting the incidence of dental caries in population groups. *J Dental Res* 1937; 16:417–30.

11. East BR. Mean annual hours of sunshine and the incidence of dental caries. *Am J Public Health Nations Health* 1939; 29:777–80.
12. Erpf SF. Dental caries and paradental disturbances. II. The seasonable incidence of dental caries. *J Am Dent Assoc* 1938; 25:681–2.
13. Hadjimarkos D, Storvick CA, Sullivan JH. Geographic variations of dental caries in Oregon III. *Oral Surg, Oral Med and Oral Path* 1950; 3:481–91.
14. Hadjimarkos DM, Storvick CA. Geographic variations of dental caries in Oregon: V. Dental caries among school children in the Willamette Valley region. *Am J Public Health Nations Health* 1951; 41:1052–8.
15. Hadjimarkos DM. Geographic variations of dental caries in Oregon VII. Caries prevalence among children in the Blue Mountains region. *J Pediatr* 1956; 48:195–201.
16. East BR. Some epidemiological aspects of tooth decay. *Am J Pub Health* 1942; 32:1242–50.
17. Blackerby PF. Intrastate geographic variations in dental caries rates. *J Am Dent Assoc* 1943; 30:1241.
18. The Michigan Workshop on the Evaluation of Dental Caries Control Techniques. *J Am Dent Assoc* 1948; 36:3.
19. Witkop CJ Jr, Barros L, Hamilton PA. Geographic and nutritional factors in dental caries. *Public Health Rep* 1962; 77:928–40.
20. Ludwig TG, Bibby BG. Geographic variations in the prevalence of dental caries in the United States of America. *Caries Res* 1969; 3:32–43.
21. Craelius W. Comparative epidemiology of multiple sclerosis and dental caries. *J Epidemiol Community Health* 1978; 32:155–65.
22. Valentine AD, Maung UT, Sein UK, Anderson RJ, Bradnock G. Geography and dental caries. *Br Dent J* 1982; 153:55–8.
23. Powell RN. Geographic effects on dental caries prevalence and tooth loss in Australia. *Community Dent Oral Epidemiol* 1983; 11:242–5.

24. Pitts NB, Boyles J, Nugent ZJ, Thomas N, Pine CM. The dental caries experience of 11-year-old children in Great Britain. Surveys coordinated by the British Association for the Study of Community Dentistry in 2004/2005. *Community Dent Health* 2006; 23:44–57.
25. Dean HT. Some epidemiological aspects of chronic endemic dental fluorosis. *Am J Pub Health* 1936; 26:567–75.
26. Grant WB. An estimate of premature cancer mortality in the US due to inadequate doses of solar ultraviolet-B radiation. *Cancer* 2002; 94:1867–75.
27. 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.
28. Hewison M. Vitamin D and the immune system: new perspectives on an old theme. *Endocrinol Metab Clin North Am* 2010; 39:365–79.
29. Dale BA, Fredericks LP. Antimicrobial peptides in the oral environment: expression and function in health and disease. *Curr Issues Mol Biol* 2005; 7:119–33.
30. Tao R, Jurevic RJ, Coulton KK, Tsutsui MT, Roberts MC, Kimball JR, et al. Salivary antimicrobial peptide expression and dental caries experience in children. *Antimicrob Agents Chemother* 2005; 49:3883–8.
31. Altman H, Steinberg D, Porat Y, Mor A, Fridman D, Friedman M, et al. In vitro assessment of antimicrobial peptides as potential agents against several oral bacteria. *J Antimicrob Chemother* 2006; 58:198–201.
32. Ji S, Hyun J, Park E, Lee BL, Kim KK, Choi Y. Susceptibility of various oral bacteria to antimicrobial peptides and to phagocytosis by neutrophils. *J Periodontal Res* 2007; 42:410–9.

Fluorosis data were obtained from a map in a paper by Dean²⁵ showing locations throughout the United States where mottled enamel (fluorosis) had been reported in the literature or reported but not verified as of 1935. The regions with the highest density of locations were generally in the southwest (Arizona, Colorado, New Mexico and Texas), as well as North and South Dakota and Iowa. Very few states in the eastern US had mottling. The fluorosis index for each state was estimated by considering the density of data overlaid with population centers for each state. The index is, therefore, approximate.

Statistical analysis. Linear and regression analyses were carried out using SPSS 16.0; Graduate Student Version (SPSS, Inc., Chicago, IL). Graphs and additional analyses were made using Kaleida Graph version 4.0 (Synergy Software, Reading, PA).

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33. Komatsuzawa H, Ouhara K, Kawai T, Yamada S, Fujiwara T, Shiba H, et al. Susceptibility of periodontopathogenic and cariogenic bacteria to defensins and potential therapeutic use of defensins in oral diseases. *Curr Pharm Des* 2007; 13:3084-95.
34. Diamond G, Beckloff N, Ryan LK. Host defense peptides in the oral cavity and the lung: similarities and differences. *J Dent Res* 2008; 87:915-27.
35. de Sousa Gomes P, Fernandes MH. Defensins in the oral cavity: distribution and biological role. *J Oral Pathol Med* 2010; 39:1-9.
36. Liu PT, Stenger S, Tang DH, Modlin RL. Cutting Edge: Vitamin D-mediated human antimicrobial activity against *Mycobacterium tuberculosis* is dependent on the induction of cathelicidin. *J Immunol* 2007; 179:2060-3.
37. Grant WB, Giovannucci D. The possible roles of solar ultraviolet-B radiation and vitamin D in reducing case-fatality rates from the 1918–1919 influenza pandemic in the United States. *Dermato-Endocrinology* 2009; 1:215-9.
38. Manaseki-Holland S, Qader G, Isaq Masher M, Bruce J, Zulf Mughal M, Chandramohan D, et al. Effects of vitamin D supplementation to children diagnosed with pneumonia in Kabul: a randomised controlled trial. *Trop Med Int Health* 2010; 15:1148-55.
39. Mookherjee N, Rehaume LM, Hancock RE. Cathelicidins and functional analogues as antiseptic molecules. *Expert Opin Ther Targets* 2007; 11:993-1004.
40. Grant WB. Solar ultraviolet-B irradiance and vitamin D may reduce the risk of septicemia. *Dermato-Endocrinology* 2009; 1:37-42.
41. Jeng L, Yamshchikov AV, Judd SE, Blumberg HM, Martin GS, Ziegler TR, Tangpricha V. Alterations in vitamin D status and anti-microbial peptide levels in patients in the intensive care unit with sepsis. *J Transl Med* 2009; 7:28.
42. Grant WB, Boucher BJ. Are Hill's criteria for causality satisfied for vitamin D and periodontal disease? *Dermato-Endocrinology* 2010; 2:30-6.
43. Boggess KA, Espinola JA, Moss K, Beck J, Offenbacher S, Camargo CA. Vitamin D status and periodontal disease among pregnant women. *J Periodontol* 2011 Feb; 82(2): 195-200.
44. Grant WB. Relation between prediagnostic serum 25-hydroxyvitamin D level and incidence of breast, colorectal and other cancers. *J Photochem Photobiol B* 2010; 101:130-6.
45. Sabetta JR, DePetrillo P, Cipriani RJ, Smardin J, Burns LA, Landry ML. Serum 25-hydroxyvitamin D and the incidence of acute viral respiratory tract infections in healthy adults. *PLoS One* 2010; 5:11088.
46. Parker J, Hashmi O, Dutton D, Mavrodaris A, Stranges S, Kandala NB, et al. Levels of vitamin D and cardiometabolic disorders: systematic review and meta-analysis. *Maturitas* 2010; 65:225-36.
47. Holick MF. Vitamin D deficiency. *N Engl J Med* 2007; 357:266-81.
48. Bartoszewska M, Kamboj M, Patel DR. Vitamin D, muscle function and exercise performance. *Pediatr Clin North Am* 2010; 57:849-61.
49. Annweiler C, Schott AM, Berrut G, Chauviré V, Le Gall D, Inzitari M, et al. Vitamin D and ageing: neurological issues. *Neuropsychobiology* 2010; 62:139-50.
50. Grant WB. In defense of the sun: An estimate of changes in mortality rates in the United States if mean serum 25-hydroxyvitamin D levels were raised to 45 ng/mL by solar ultraviolet-B irradiance. *Dermato-Endocrinology* 2009; 1:207-14.
51. Grant WB, Schwalfenberg GK, Genuis SJ, Whiting SJ. An estimate of the economic burden and premature deaths due to vitamin D deficiency in Canada. *Molec Nutr Food Res* 2010; 54:1127-33.
52. Grant WB, Juzeniene A, Moan JE. Health benefit of increased serum 25(OH)D levels from oral intake and ultraviolet-B irradiance in the Nordic countries. *Scand J Public Health* 2011; 39:70-8.
53. Norman AW, Bouillon R. Vitamin D nutritional policy needs a vision for the future. *Exp Biol Med* (Maywood) 2010; 235:1034-45.
54. Hyppönen E, Power C. Hypovitaminosis D in British adults at age 45 y: nationwide cohort study of dietary and lifestyle predictors. *Am J Clin Nutr* 2007; 85:860-8.
55. Heaney RP, Davies KM, Chen TC, Holick MF, Barger-Lux MJ. Human serum 25-hydroxycholecalciferol response to extended oral dosing with cholecalciferol. *Am J Clin Nutr* 2003; 77:204-10.
56. Garland CF, French CB, Baggerly LL, Heaney RP. Vitamin D supplement doses and serum 25-hydroxyvitamin D in the range associated with cancer prevention. *Anticancer Res* 2011; 31:617-22.
57. Iida H, Kumar JV. The association between enamel fluorosis and dental caries in US schoolchildren. *J Am Dent Assoc* 2009; 140:855-62.
58. Bachrach LK, Hastie T, Wang MC, Narasimhan B, Marcus R. Bone mineral acquisition in healthy Asian, Hispanic, black and Caucasian youth: a longitudinal study. *J Clin Endocrinol Metab* 1999; 84:4702-12.
59. Webb AR, Kline L, Holick MF. Influence of season and latitude on the cutaneous synthesis of vitamin D3: exposure to winter sunlight in Boston and Edmonton will not promote vitamin D3 synthesis in human skin. *J Clin Endocrinol Metab* 1988; 67:373-8.
60. Dean HT, Arnold FA Jr, Jay P, Knutson JW. Studies on mass control of dental caries through fluoridation of the public water supply 1950; 65:1403-8.
61. Arnold FA Jr, Dean HT, Jay P, Knutson JW. Effect of fluoridated public water supplies on dental caries prevalence 1956. *Bull World Health Organ* 2006; 84:761-4.
62. CDC. Fluoridation census 1992. Atlanta, Georgia: US Department of Health and Human Services, Public Health Service CDC, National Center for Prevention Services, Division of Oral Health 1993.
63. [No authors listed] From the Centers for Disease Control and Prevention. Achievements in public health 1900–1999: fluoridation of drinking water to prevent dental caries. *JAMA* 2000; 283:1283-6.
64. Künzel W, Fischer T, Lorenz R, Brühmann S. Decline of caries prevalence after the cessation of water fluoridation in the former East Germany. *Community Dent Oral Epidemiol* 2000; 28:382-9.
65. Seppä L, Kärkkäinen S, Hausen H. Caries trends 1992–1998 in two low-fluoride Finnish towns formerly with and without fluoridation. *Caries Res* 2000; 34:462-8.
66. Committee on Fluoride in Drinking Water. Fluoride in Drinking Water: A Scientific Review of EPA's Standards Committee on Fluoride in Drinking Water. National Research Council, Washington DC 2006.
67. Carton RJ. Review of 2006 USNRC report on *Fluoride in drinking water*. Fluoride 2006; 39:163-72.
68. USEPA and HHS. EPA and HHS Announce New Scientific Assessments and Actions on Fluoride/Agencies working together to maintain benefits of preventing tooth decay while preventing excessive exposure. Jan. 7, 2011; <http://yosemite.epa.gov/opa/admpress.nsf/d0cf6618525a9efb85257359003fb69d/86964af577c37ab285257811005a8417?OpenDocument>
69. McDonagh MS, Whiting PF, Wilson PM, Sutton AJ, Chestnutt I, Cooper J, et al. Systematic review of water fluoridation. *BMJ* 2000; 321:855-9.
70. Pizzo G, Piscopo MR, Pizzo I, Giuliana G. Community water fluoridation and caries prevention: a critical review. *Clin Oral Investig* 2007; 11:189-93.
71. Grant WB, Garland CF, Holick MF. Comparisons of estimated economic burdens due to insufficient solar ultraviolet irradiance and vitamin D and excess solar UV irradiance for the United States. *Photochem Photobiol* 2005; 81:1276-86.
72. Grant WB. Hypothesis—ultraviolet-B irradiance and vitamin D reduce the risk of viral infections and thus their sequelae, including autoimmune diseases and some cancers. *Photochem Photobiol* 2008; 84:356-65.
73. Grant WB. The prevalence of multiple sclerosis in 3 US communities: the role of vitamin D [letter]. *Prev Chronic Dis* 2010; 7:89.