Review Article

Relationships of Blood Lead Concentrations to Vitamin D, Season of Year, Sunlight Exposure, and Linear Growth in Children

Catherine Chen[1], James M. Oleske[2], Anthony J. Scolpino[2], Ronnie Levin[3], Hernan F. Gomez[4] and John D. Bogden[5,6]*

[1]Northwestern University, USA

[2]Department of Pediatrics, Rutgers New Jersey Medical School, USA.

[3]Department of Environmental Health, Harvard School of Public Health, USA

[4]Department of Emergency Medicine, University of Michigan and Department of Emergency Medicine, Hurley Medical Center, USA

[5]Department of Microbiology, Biochemistry, and Molecular Genetics, Rutgers New Jersey Medical School, USA

ARTICLE INFO

Received Date: May 20, 2022
Accepted Date: June 13, 2022
Published Date: June 15, 2022

KEYWORDS

Vitamin D
Children
Growth
Adults
Lead
Season
Sunlight

Citation for this article: Catherine Chen, Oleske JM, Scolpino AJ, Levin R, Gomez HF and Bogden JD. Relationships of Blood Lead Concentrations to Vitamin D, Season of Year, Sunlight Exposure, and Linear Growth in Children. SL Nutrition And Metabolism. 2022; 2(1):122

[6]***Corresponding author:**
Bogden JD,
Department of Microbiology, Biochemistry, and Molecular Genetics, International Center for Public Health Building, 225 Warren Street, Third Floor, Room E350V, Newark, NJ, 07101-3535, USA, Tel: +973-972-5432;
Email: john.bogden@rutgers.edu

ABSTRACT

Design: The objective of this review is to describe and evaluate published studies that assess the relationships among linear growth, season of year, blood lead levels (BLLs), and vitamin D nutrition.

Methods/Approach: A "Keyword" search of PubMed and Medline databases was performed to identify all relevant papers published in peer-reviewed journals.

Results: The majority of the studies reviewed reported a seasonal variation in linear growth. Children living at higher latitudes were found to exhibit the greatest growth velocities during the warmest months, possibly due to the fact that at higher latitudes they experience a greater increase in daylight hours and greater sunlight exposure during warmer compared to colder months. While sunlight exposure may play a role in the seasonal variation of linear growth, there was no significant association between increases in height and sunlight-induced changes in serum 25-hydroxy-vitamin D concentrations. However, BLLs were significantly associated with serum-25-hydroxy-vitamin D concentrations. Although both linear growth and BLLs increase during warmer months of the year, bone turnover rates do not follow the same seasonal pattern, suggesting that greater linear growth in the summer does not increase the release of lead from bone into the bloodstream.

Conclusion: While the present study confirms the seasonality of linear growth, serum 25-hydroxy- vitamin D concentrations, and BLLs in children, a causal relationship between decreased linear growth and higher blood lead concentrations or between increased linear growth and higher serum 25-hydroxy-vitamin D concentrations cannot be confirmed.

INTRODUCTION

Lead exposure can cause potentially permanent cognitive and behavioural impairments, especially in children [1]. High Blood Lead Levels (BLLs) during childhood have also been reported to cause later pubertal onset [2,3] and have been linked to lower height and weight [4,5]. While BLLs in children have declined substantially worldwide due to the identification and removal of some of the sources of lead exposure, a distinct seasonal variation of BLLs and the incidence of elevated BLLs persists [6,7]. Specifically, BLLs of children tend to be higher during warmer months than colder months of the year [8-10]. The seasonal variation of blood lead concentrations has been attributed to increased outdoor activity by young children during warmer weather, leading to increased exposure to lead-contaminated air, street dust, and soil [7-11]. The increase in sunlight-induced vitamin D synthesis in the summer has also been suggested as an explanation, as vitamin D may promote gastrointestinal lead absorption in addition to its well-documented ability to increase calcium absorption [12,13].

While increased lead exposure during childhood has been associated with reduced height [14], we hypothesize that greater linear growth in the summer increases the release of lead from bone into the bloodstream and is the primary cause of the well-documented increase in blood lead concentrations during the summer. Additionally, because adults are not growing, we suggest that there is little to no increase in adult blood lead concentrations in the summer.

In order to investigate these hypotheses and the causes of seasonal variation in BLLs, we conducted a review of published studies. We aimed to answer the following questions:

(1) Is the linear growth of boys and girls greater in the summer than during other seasons of the year?

(2) Is sunlight-induced Vitamin D synthesis during the summer a factor that increases linear growth and/or blood lead concentrations in children?

(3) Is there evidence that the summer increase in blood lead concentrations is caused by greater linear growth in the summer?

(4) Do blood lead concentrations in adults increase during the summer?

METHODS

A search of PubMed and Medline databases was performed to identify all relevant papers published in peer-reviewed journals. The following key terms, Medical Subject Headings (MeSH) and the Boolean operators, AND and OR, were used in a variety of combinations in our search strategy: ("growth" OR "growth and development" OR "body height" OR "anthropometry") AND ("child" OR "adolescent") AND "seasons" AND ("bones" OR "bone remodeling" OR "bone resorption" OR "osteoporosis") AND ("lead" OR "lead poisoning" OR "blood lead") AND ("vitamin D" OR "sunlight") AND "adult." In addition to the online search, a manual search of reference lists was performed to find other relevant articles. No limits were applied to the time of publication.

RESULTS AND DISCUSSION

Articles reviewed

After excluding duplicates, a total of 807 potentially relevant articles were identified by the literature search (Figure 1). Of those, 754 articles were excluded after examining their titles, abstracts, and keywords. Of the remaining 53 articles, 22 papers were excluded due to insufficient data and/or lack of relevance to answering the four key questions of our study. Finally, 31 articles were included and further analyzed in this review (Figure 1).

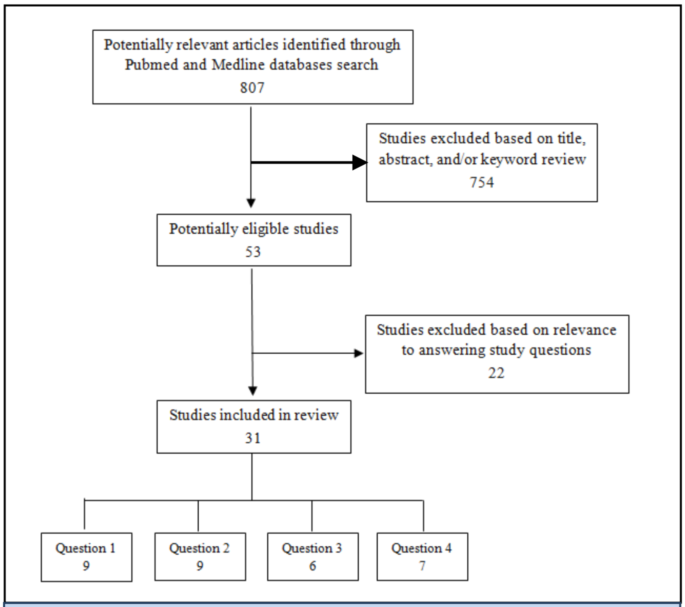

Figure 1: Flow chart of study selection.

Seasonality of linear growth in children

The existing scientific literature on seasonality of growth supports the claim that the linear growth of children is greater in the spring and summer months than during other seasons of the year. The earliest observations of this phenomenon date back to the 1940s, with the greatest height increases in normal, prepubertal children occurring most frequently between the months of March and July [15,16]. In one of these studies (15) 130 children (65 males and 65 females) were monitored for growth from age 12-60 months, including with lower limb X-rays taken at 6-month intervals on their birthdays and "halfbirthdays" to provide data on ossification. A confounding factor in this study is that the children's birthdays occurred throughout the year and often not in the winter or summer seasons; this may have reduced but did not prevent detection of seasonal effects on growth. The other study of English children (16) attending seasonal "camps" revealed that growth in one season influences growth in subsequent seasons and demonstrated that young children have a "resilience" that enables seasons of greater than average growth subsequent to seasons of low growth. The authors suggest that resilience is one reason for the variability of seasonal growth of children.

A 1971 paper (17) includes data on linear growth of 260 "well-nourished" older children aged 7-10 years measured at one-month intervals for 13 months. Maximal 3-month rates of growth occurred in the spring/summer months from March to July and the slowest growth occurred in the fall/winter months between September and February. The growth rates during the spring and summer months were reported to be approximately 2 to 3 times, and occasionally up to 7 times, the slowest growth rate during the winter months [17].

This seasonal variation in growth was also observed in children with growth hormone deficiency; two studies showed that there was significant seasonal variability at all latitudes with the growth velocity in the summer greater than that in the winter ($p<0.001$; n=2277) in these children [18,19]. Interestingly, De Leonibus et. al [19] found that growth hormone deficient children living at higher latitudes and thus experiencing a greater increase in daylight hours during the summer were found to have the highest growth rates, suggesting a role for sunlight exposure in child growth ($r=0.256$; $p=0.006$; n=118). However, the association, though statistically significant, is weak because only 6.6% of the variability in linear growth was explained by greater sunlight exposure.

Though the majority of the scientific literature reports seasonal differences in growth, some studies did not find associations between season of the year and growth rates [20,21]. However, it is important to consider that few studies measured children's statures during holidays or summer vacations and that children living in tropical climates experience minimal changes in sunlight exposure, which may be a factor in linear growth. For example, children in temperate climates exhibit clear seasonal variation in growth, and they experience a faster growth velocity in the spring and summer. On the other hand, children living in the tropics experience faster growth velocities in the dry season, which does not necessarily occur during the spring and summer months, but rather when sun exposure is the greatest [22]. Another relevant issue is that most studies observe higher growth velocities in the spring and summer in large populations, but these trends only approximately reflect individual growth patterns, and growth of individual children often fails to conform to these general seasonal patterns [23].

Sunlight-induced vitamin D synthesis and linear growth

Various studies have found associations between increased amounts of sunlight exposure and greater linear growth velocity of children, and it is possible that sunlight-induced vitamin D synthesis may explain this increase in growth [18,22]. Although a majority of studies observe that serum 25-hydroxyvitamin D levels (of which 90% is vitamin D3) and linear growth exhibit a similar seasonal variation, with higher vitamin D levels in the spring and summer seasons, there is insufficient evidence to conclude that vitamin D is a factor in increasing linear growth in children.

Several studies assessing serum 25-hydroxy-vitamin D concentrations and anthropometric variables reported no significant association between height and vitamin D concentrations [24-26]. Dong et al [24] found that serum 25-hydroxy-vitamin D was not associated with height in 14 to 18-year-old African-American and white children in the south eastern United States ($p=0.139$; n=559). Sayers et al [25] assessed 3,579 children age 7 to 12-years from the Avon Longitudinal Study of Parents and Children and found little association between height and vitamin D concentrations. Serum 25-hydroxy-vitamin D levels were even found to be inversely related to bone mineral accrual rates, which peak in conjunction with linear growth velocity [27]. In contrast, one study of Australian women ages 16-25 years old found a strong positive association between serum 25-hydroxy-vitamin D levels and height ($r=0.70$; $p=0.016$; n=348) [28].

Vitamin D3 supplementation studies provide additional evidence. Ganmaa et al [29] studied Mongol children ages 6-8 years old with very low serum 25-hydroxyvitamin D concentrations in the winter who were randomly assigned to a placebo group or a group consuming 800 IU of vitamin D3 for 6 months. A positive effect on linear growth was observed for children who had consumed vitamin D supplements, and they experienced a 0.90 cm greater increase in height compared to placebo-treated participants ($p=0.003$; $n=113$). However, a weakness of this study is that the diets of the children, including calories and vitamin D consumed, were not formally assessed.

Not all studies done demonstrate that linear growth in children differs by season. In a study of 115 blind children and 309 normally sighted children, normally-sighted children reached maximal growth rates during the summer, but blind children exhibited no seasonal variation in growth and had peak growth rates at various times throughout the year [30]. If vitamin D3 played a significant role in growth, then the fact that the children were blind would most likely not affect vitamin D3 synthesis, which occurs in the skin. However, it is possible that the blind children spent less time outdoors, which may have accounted for their lack of seasonality in growth.

While an increase in dietary and/or supplemental vitamin D is required to achieve genetic growth potential in children with moderate to severe deficiencies [29], the role of supplemental vitamin D in linear growth of children with mild deficiencies may be too small and/or masked by other factors, such as physical activity and melatonin synthesis [24,31-32].

Season, blood lead, bone turnover, and linear growth

Most of the body lead burden is stored in the bones, 90-95% in adults and 73% in children. During times of increased bone turnover, such as pregnancy, lactation, menopause [32-34] and rapid growth in childhood [35-37], more lead is released from bone stores, thereby increasing BLLs. However, even though linear growth in children increases in the spring and summer months, we found no evidence that suggests that greater linear growth is the cause of increased BLLs in the summer.

There is conflicting data regarding the seasonality in bone turnover in children. In a study of 6 to 12-year-old African-American and white children, CTx, a bone marker for resorption, was found to be lower in the summer (0.7 ng/mL) and significantly higher in the winter (1.0 ng/mL) in African-American children ($p<0.001$; $n=82$) [38]. Another study of 10-year-old German children mirrored these results, reporting a clear seasonal variation of bone turnover markers with a 10 nmol/L increase in serum vitamin D concentrations associated with a significant decrease of -10.5 ng/L in CTx ($p<0.001$; $n=2798$) [35]. Conversely, a study of 11-year-old Finnish girls reported that osteocalcin, a biomarker of bone formation, was 17.6% lower in March, which is considered late winter, than in September, which is considered the end of summer ($p<0.01$; $n=196$). It is important to note that the study was conducted from September to March, and no data was collected during the spring and summer months (April-August) due to school vacation [39]. If linear growth did influence BLLs, there would be increased bone turnover associated with increased growth during the summer months. The results of these studies are inconsistent and do not provide conclusive evidence that supports greater linear growth as the cause of higher BLLs of children in the summer.

There were no studies that examined both seasonal changes in blood lead concentrations and in linear growth in the same population. However, a significant negative correlation between blood lead concentrations of 5-35 ug/dL and growth and stature was observed in several studies [40-42]. Using data from the Second National Health and Nutrition Examination Survey (NHANES II), Schwartz et al [40] examined the association between anthropometric variables and BLLs in children 6 months to 7 years of age. BLLs were found to be a statistically significant predictor of children's height, and higher BLLs of children were associated with a reduction of about 1.5% in height ($p<0.001$; $n=2,695$). Burns et al [41] assessed peripubertal Russian boys ages 8 to 9-years-old and continued measurements annually for 10 years. Boys with higher BLLs (>5 ug/dL) compared to lower BLLs were significantly shorter over the 10 years of follow-up, translating to a height lower by 2.5 cm at 18 years of age ($p<0.001$; $n=481$). Another study by Little et al [42] analyzed BLLs and growth status of children ages 2 to 12-years-old living in Texas lead smelter communities and found that higher blood lead levels were associated with lower age- and sex-specific height z-scores ($p<0.0001$; $n=360$).

While bone turnover is positively associated with growth rate, there is no evidence that bone turnover and growth rate show the same seasonal variation.

Blood lead concentrations in adults

The current scientific literature on blood lead is mostly focused on children rather than adults. The few articles about adult BLLs present conflicting results. Solé et al [43] examined BLLs in individuals 15 to 62-years-old living in the Metropolitan Area of Barcelona and found that those who had their blood sampled in the warmer months had higher BLLs, but their BLLs were not significantly greater than those of study subjects sampled during different seasons ($F=0.257$; $p>0.05$; $n=254$). Watanabe et al [44] assessed Japanese farmers in 14 regions on two successive occasions, once in a winter and once in the immediately preceding or succeeding summer. They found that the difference between paired values of blood lead of individual farmers was not statistically significant ($p>0.05$; $n=506$) even though the BLLs were usually higher in the summer than winter. Interestingly, when the winter and summer measurements were stratified by sex, the summer BLLs in females were significantly higher than the winter BLLs ($p<0.01$; $n=283$), but there was no statistically significant difference in males ($p>0.05$; $n=222$).

One study found that bone turnover markers in adults were significantly higher in the winter months than during warmer weather ($p<0.01$; $n=580$) [45], and another study of 21 to 80-year-old males reported higher mean BLLs in the winter (6.6 ug/dL) than in the spring and summer (5.8 ug/dL and 6.1 ug/dL, respectively). The study also found that mean bone lead levels were higher in the summer (23.9 ug/g) than in the winter (20.3 ug/g), suggesting that bone releases more lead into the blood during the winter. In the study's full regression model of blood lead, the interaction terms for season with bone lead were highly significant ($p<0.0001$; $n=764$) [46]. However, a weakness of this investigation was that the men studied in summer were not the same men who were studied during winter.

Though it is unclear whether adults in general show seasonal variation in blood lead concentrations, some studies demonstrate that pregnant women exhibit increased BLLs in the winter and decreased BLLs in the summer. Farias et al [47] assessed BLLs of pregnant women in Mexico City and found that the lowest mean BLLs occurred in the summer (4.7 ug/dL) compared to the winter (12.7 ug/dL) ($p<0.01$; $n=513$). Another study of pregnant women in New York found that the highest BLLs occurred from December to March ($p<0.05$; $n=188$) [48]. This seasonal effect has been attributed to increased mobilization of bone lead stores during winter caused by decreased exposure to sunlight, lower levels of activated vitamin D, and enhanced bone resorption [49].

Thus, while the seasonal effect on children's BLLs is well-established, there is insufficient evidence to conclude that blood lead concentrations in adults increase during the summer.

Recent studies of vitamin D deficiency in children

A very large ($n = 151{,}705$) recently published study of children and adults living in Lebanon [50] confirms the seasonal pattern of serum 25-hydroxy-vitamin D concentrations. A multivariate analysis of this large data set identified winter season as a significant predictor of extremely low (< 12 ng/ml), very low (12 to < 15 ng/ml), and low (15 to < 20 ng/ml) serum 25-hydroxy-vitamin D concentrations. Another recent study reveals the high frequency of low serum 25-hydroxy-vitamin D concentrations in 6,896 Chinese children age 6-36 months [51] who had a positive (20.7 % deficient) or negative (12.1% deficient) H-pylori serum antibody test.

A recent American Academy of Pediatrics (AAP) report [52] focused on dietary vitamin D intakes of infants from birth to age 11 months. Overall, only 27.1% of the infants, whether breast fed or not, had intakes ≥ 400 IU of vitamin D, the AAP dietary guideline for infants. The study revealed only minor changes in the percent of infants meeting the guideline during the seven-year period of 2009-2016. The above three studies reveal that vitamin D deficiency in children continues to be common and widespread in Lebanon, China, and the United States, and suggest that it is also likely to be common in many other countries, especially during the winter.

CONCLUSION

The present review assesses the relationships among linear growth, season of year, blood lead, and vitamin D nutritional status. In this review, we found no studies analyzing seasonal changes in BLLs and changes in linear growth in the same population. However, higher BLLs are associated with lower height in children [40-42]. Future studies examining seasonal variation in both BLLs and linear growth are needed.

Although the present study confirms the seasonality of both linear growth and BLLs in children, a causal relationship cannot be established between decreased linear growth and increased blood lead concentrations or between increased linear growth and increased serum 25-hydroxy-vitamin D concentrations. We did not address previous BLL status and its relationship to the extent of change in BLLs from colder to warmer months, because Ngueta et al [53] have examined this issue in depth. We think that it is unlikely that greater outdoor exposure of children to lead in the summer is the sole factor responsible for the seasonal variation in blood lead. We suggest that factors, such as diet composition, increased physical activity, and melatonin synthesis may each contribute to the seasonal changes in blood lead concentrations, and the potential role of vitamin D should be further investigated [54]. Developing a comprehensive and definitive explanation for the increase in blood lead levels of children in the warmer months will require additional exploration.

REFERENCES

1. Hou S, Yuan L, Jin P, Ding B, Qin N, et al. (2013). A clinical study of the effects of lead poisoning on the intelligence and neurobehavioral abilities of children. Theor Biol Med Model. 10:13.
2. Hauser R, Sergeyev O, Korrick S, Lee MM, Revich B, et al. (2008). Association with BLLs with onset of puberty in Russian boys. Environ Health Perspect. 116: 976-980.
3. Selevan SG, Rice DC, Hogan KA, Euling SY, Pfahles-Hutchens A, et al. (2003). Blood lead concentration and delayed puberty in girls. N Engl J Med. 348: 1527-1536.
4. Ballew C, Khan LK, Kaufmann R, Mokdad A, Miller DT, et al. (1999). Blood lead concentration and children's anthropometric dimensions in the Third National Health and Nutrition Examination Survey (NHANES III), 1988-1994. J Pediatr. 134: 623-630.
5. Kafourou A, Touloumi G, Makropoulos V, Loutradi A, Papanagiotou A, et al. (1997). Effects of lead on the somatic growth of children. Arch Environ Health. 52: 377-383.
6. Laidlaw MAS, Mielke HW, Filippelli GM, Johnson DL, Gonzales CR. (2005). Seasonality and children's BLLs: developing a predictive model using climatic variables and blood lead data from Indianapolis, Indiana, Syracuse, New York, and New Orleans, Louisiana. Environ Health Perspect. 113: 793-800.
7. Yiin LM, Rhoads GC, Lioy PJ. (2000). Seasonal influences on childhood lead exposure. Environ Health Perspect. 108: 177-182.
8. Hunter JM. (1977). The summer disease: an integrative model of the seasonality aspects of childhood lead poisoning. Soc Sci Med. 11: 691-703.
9. Rothenberg SJ, Williams FA Jr, Delrahim S, Khan F, Kraft M, et al. (1996). BLLs in children in south central Los Angeles. Arch Environ Health. 51: 383-388.
10. Stark AD, Quah RF, Meigs JW, de Louis ER. (1980). Season as a factor in variability of blood-lead levels in children. Conn Med. 44: 410-413.
11. Mielke HW and Reagan PL. (1998). Soil is an important pathway of human lead exposure. Environ Health Perspect. 106: 217-229.
12. Kemp FW, Neti PV, Howell RW, Wenger P, Louria DB, et al. (2007). Elevated blood lead concentrations and vitamin D deficiency in winter and summer in young urban children. Environ Health Perspect. 115: 630-635.
13. Peraza MA, Ayala-Fierro F, Barber DS, Casarez E, Rael LT. (1998). Effects of micronutrients on metal toxicity. Environ Health Perspect. 106: 203-216.
14. Ignasiak Z, Slawinska T, Rozek K, Little BB, Malina RM. (2006). Lead and growth status of school children living in the copper basin of south-western Poland: differential effects on bone growth. Ann Hum Biol. 33: 401-414.
15. Reynolds EL, Sontag LW. (1944). Seasonal variations in weight, height and appearance of ossification centres. Journal of Pediatrics. 24: 524-535.
16. Bransby ER. (1945). The seasonal growth of children. Medical Officer. 73: 149-165.
17. Marshall W. (1971). Evaluation of growth rate in height over periods of less than one year. Arch Dis Child. 46: 414-420.
18. Shulman DI, Frane J, Lippe B. (2013). Is there 'seasonal' variation in height velocity in children treated with growth hormone? Data from the National Cooperative Growth Study. Int J Pediatr Endocrinol. 2013: 2.
19. De Leonibus C, Chatelain P, Knight C, Clayton P, Stevens A. (2016). Effect of summer daylight exposure and genetic background on growth in growth hormone-deficient children. Pharmacogenomics J. 16: 540-550.
20. Siniarska A, Rojas A, Valentin G, Wolanski N. (2009). Does a seasonal developmental rhythm exist in tropical living populations? Coll Anthropol. 33: 709-724.
21. Ikeda M, Watanabe T. (1985). Constant growth of primary school children throughout four seasons of year. Tohoku J Exp Med. 145: 413-418.

22. Schell L, Knutson K, Bailey S. (2012). Human growth and development. 2nd ed. Academic Press. Chapter 10, Environmental Effects on Growth. p245-286.
23. Tillmann V, Thalange NK, Foster PJ, Gill MS, Price DA, et al. (1998). The relationship between stature, growth, and short-term changes in height and weight in normal prepubertal children. Pediatr Res. 44: 882-886.
24. Dong Y, Pollock N, Stallmann-Jorgensen IS, Gutin B, Lan L, et al. (2010). Low 25-hydroxyvitamin D levels in adolescents: race, season, adiposity, physical activity, and fitness. Pediatrics. 125: 1104-1111.
25. Sayers A, Fraser W, Lawlor D, et al. (2012). 25-Hydroxyvitamin-D3 levels are positively related to subsequent cortical bone development in childhood: findings from a large prospective cohort study. Osteoporosis Int. 23: 2117–2128.
26. Geng SS, Ma JQ, Liu SS, Zhang J, Sheng XY. (2016). Vitamin D insufficiency and its association with biochemical and anthropometric variables of young children in rural southwestern China. Chin Med J. 129: 1273-1279.
27. Breen ME, Laing EM, Hall DB, Hausman DB, Taylor RG, et al. (2011). 25-hydroxyvitamin D, insulin-like growth factor-I, and bone mineral accrual during growth. J Clin Endocrinol Metab. 96: E89–E98.
28. Callegari ET, Garland SM, Gorelik A, Reavley NJ, Wark JD. (2017). Predictors and correlates of serum 25-hydroxyvitamin D concentrations in young women: results from the Safe-D study. Br J Nutr. 118: 263-272.
29. Ganmaa D, Stuart JJ, Sumberzul N, Ninjin B, Giovannucci E, et al. (2017). Vitamin D supplementation and growth in urban Mongol school children: Results from two randomized clinical trials. PLoS One. 12: e0175237.
30. Marshall WA, Swan AV. (1971). Seasonal variation in growth rates of normal and blind children. Hum Biol. 43: 502-516.
31. Yokoya M, Shimizu H, Higuchi Y. (2012). Geographical distribution of adolescent body height with respect to effective day length in Japan: An ecological analysis. PLoS One. 7: e50994.
32. Potula V, Henderson A, Kaye W. (2005). Calcitropic hormones, bone turnover, and lead exposure among female smelter workers. Arch Environ Occup Health. 60: 195-204.
33. Silbergeld EK, Schwartz J, Mahaffey K. (1998). Lead and osteoporosis: Mobilization of lead from bone in postmenopausal women. Environ Res. 47: 79-94.
34. Machida M, Sun SJ, Oguma E, Kayama F. (2009). High bone matrix turnover predicts blood levels of lead among perimenopausal women. Environ Res. 109: 880-886.
35. Thiering E, Bruske I, Kratzch J, Hofbauer LC, Berdel D, et al. (2015). Associations between serum 25-hydroxyvitamin D and bone turnover markers in a population based sample of German children. Sci Rep. 5.
36. van Coeverden SC, Netelenbos JC, de Ridder CM, Roos JC, Popp-Snijders C, et al. (2002). Bone metabolism markers and bone mass in healthy pubertal boys and girls. Clin Endocrinol (Oxf). 57: 107-116.
37. Tarragó O, Brown MJ. (2018). “Lead Toxicity.” ATSDR Case Studies in Environmental Medicine.
38. Rajakumar K, Holick MF, Moore CG, Cohen E, Olabopo F, et al. (2014). Impact of seasonal flux on 25-hydroxyvitamin D and bone turnover in pre- and early pubertal youth. Pediatr Int. 56: 35-42.
39. Viljakainen HT, Palssa A, Kärkkäinen M, Jakobsen J, Cashman KD, et al. (2006). A seasonal variation of calcitropic hormones, bone turnover and bone mineral density in early and mid-puberty girls - a cross-sectional study. Br J Nutr. 96: 124-130.
40. Schwartz J, Angle C, Pitcher H. (1986). Relationship between childhood BLLs and stature. Pediatr. 77: 281-288.
41. Burns JS, Williams PL, Lee MM, Revich B, Sergeyev O, et al. (2017). Peripubertal BLLs and growth among Russian boys. Environ Intr. 106: 53-59.
42. Little BB, Snell LM, Johnston WL, Knoll KA, Buschang PH. (1990). BLLs and growth status in children. Am J Hum Biol. 2: 265-269.
43. Solé E, Ballabriga A, Dominguez C. (1998). Lead exposure in the general population of the Metropolitan Area of Barcelona: blood levels and related factors. Sci Total Environ. 224: 19-27.
44. Watanabe T, Fujita H, Koizumi A, Chiba K, Miyasaka M, et al. (1985). Baseline level of blood lead concentration

among Japanese farmers. Arch Environ Health. 40: 170-176.

45. Woitge HW, Scheidt-Nave C, Kissling C, Leidig-Bruckner G, Meyer K, et al. (1998). Seasonal variation of biochemical indexes of bone turnover: results of a population-based study. J Clin Endocrinol Metab. 83: 68-75.
46. Oliveira S, Aro A, Sparrow D, Hu H. (2002). Season modifies the relationship between bone and BLLs: the normative aging study. Arch Environ Health. 57: 466-472.
47. Farias P, Borja-Aburto VH, Rios C, Hertz-Picciotto I, Rojas-Lopez M, et al. (1996). BLLs in pregnant women of high and low socioeconomic status in Mexico City. Environ Health Perspect. 104: 1070-1074.
48. Schell LM, Stark AD, Gomez MI, Grattan WA. (1997). Blood lead level, by year and season. Arch Environ Health. 52: 286-291.
49. Salari P, Abdollahi M. (2014). The influence of pregnancy and lactation on maternal bone health: a systematic review. J Family Reprod Health. 8: 135-148.
50. Saad RK, Akiki VC, Rahme M, Ajjour S, Assaad M, et al. (2020). Time trends and predictors of hypovitaminosis D across the life course: 2009-2016 Metabolism Clinical and Experimental 105: 154138.
51. Gao T, Zhao M, Zhang C, Wang P, Zhou W, Tan S, et al. (2020). Association of Helicobacter Pylori infection with vitamin D deficiency in infants and toddlers. Amer J Trop Med Hyg. 102: 541-546.
52. Simon A, Aherns KA. (2020). Adherence to vitamin D intake guidelines in the United States. Pediatrics. 145: e2019357.
53. Ngueta G, Gonthier C, Levallois P. (2015). Colder-to-warmer changes in children's blood lead concentrations are related to previous blood lead status: Results from a systematic review of prospective studies. J Trace Elements Med Biol. 29: 39-46.
54. Levin R, Zilli Vieira CL, Modarski DC, Rosenbaum MH. (2020). Lead seasonality in humans, animals, and the natural environment. Environ Res 180: 1-11.