Clinical Pediatrics
Volume XX Number X
Month XXXX xx-xx

10.1177/0009922807311397
http://clp.sagepub.com
hosted at
http://online.sagepub.com

10-Year Case Review of Nutritional Rickets in Children's Hospital of Michigan

Judith P. Lazol, MD,[1] Nedim Çakan, MD,[2] and Deepak M. Kamat, MD, PhD[2]

Nutritional rickets has been on the rise in the United States. A chart review of patients with nutritional rickets from April 1995 to May 2005 was performed. Fifty-eight subjects were studied (62% males, 38% females, with an age range between 2 and 132 months). Of the subjects, 81% were African Americans and 14% were Arabic; 33% were Christians and 19% were Muslims. An increasing number of cases of nutritional rickets have been noted since 2000. Seventy-nine percent of patients with nutritional rickets presented at the emergency department, and in 69% of the cases, rickets was an incidental finding; 96% of patients were exclusively breast-fed, and none received multivitamin supplements. 25-OH vitamin D levels were below 5 ng/mL in 42% of the patients, all of whom were African Americans. We could document complete resolution of nutritional rickets in only 8 patients, and 3 of these patients showed sequelae of rickets.

Keywords: nutritional rickets; vitamin D; vitamin D 25(OH); vitamin D 1,25 (OH); breast-feeding; vitamin D supplementation

Introduction

Rickets, once virtually eradicated in the United States, has reemerged as a public health issue. In addition to the acute morbidities caused by rickets, recent publications point out the long-term consequences of vitamin D deficiency, such as increased risks of type I diabetes, cancer, and osteoporosis.[1-3]

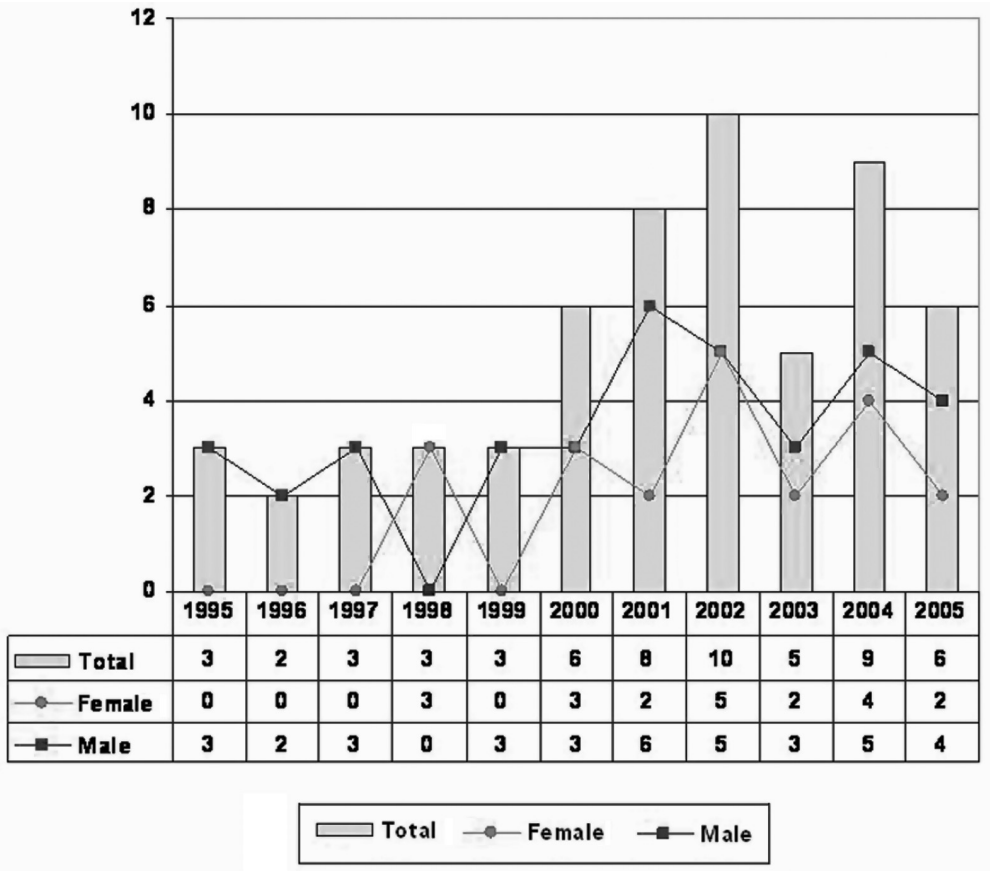
At the Children's Hospital of Michigan, there is concern about the upsurge of rickets cases.[4,5] However, except for a report from 1987, no data are available.[6] This study was conducted to assess the characteristics of nutritional rickets in this institution and to investigate factors associated for its uptrend.

From the [1]Pittsburgh Children's Hospital, Pittsburgh, Pennsylvania; and the [2]Children's Hospital of Michigan, Detroit, Michigan.

Address correspondence to: Deepak M. Kamat MD, PhD, Institute of Medical Education, Carman and Adams Department of Pediatrics, Children's Hospital of Michigan, 3901 Beaubien Boulevard, Detroit Medical Center, Detroit, MI 48201; e-mail: dkamat@med.wayne.edu.

Methods

After approval from the institutional review board, charts of cases with an *International Classification of Diseases*, ninth revision, code of 268.0 (diagnosis code for rickets) as the principal or secondary diagnosis between April 1995 and May 2005 at the Children's Hospital of Michigan were reviewed. Only nutritional rickets were included. Cases with radiological findings of rickets without laboratory data supporting the diagnosis of rickets were not included. Variables such as age at diagnosis, gender, race, and feeding history (past and current), as well as vitamin D and calcium supplementation, were noted. Information on history of sun exposure and use of sunblock lotion, religious beliefs, month and year of diagnosis, and place (emergency department [ED] or clinic) where the diagnosis of rickets was established were reviewed. Clinical signs of rickets, growth parameters, and laboratory evaluations, such as hemoglobin/hematocrit, serum levels of calcium, phosphorus, alkaline phosphatase, parathyroid hormone, and vitamin D, as well as X ray findings and information on treatment and follow-up, were also reviewed.



	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005
Total	3	2	3	3	3	6	8	10	5	9	6
Female	0	0	0	3	0	3	2	5	2	4	2
Male	3	2	3	0	3	3	6	5	3	5	4

Figure 1. Total cases of nutritional rickets (with gender ratio).

Results

Subjects

Charts of 176 subjects were retrieved, and 58 cases were included in the study. There were 36 (62%) boys and 22 (38%) girls. Patients' ages ranged from 2 to 132 months, with a mean age of 18 months (±standard deviation [SD] 19.7) and a median age of 12 months at the first diagnosis of nutritional rickets. Mean age of diagnosis for boys and girls was 21 (±SD 24) and 13 (±SD 13) months, respectively, though the difference was not statistically significant on *t*-test. Forty-six (96%) of the 48 subjects were born full-term, and the remaining 2 were born at 34 weeks of gestation. Data regarding maternal intake of multivitamins during pregnancy and lactation were not available. A breakdown of cases seen per year is shown in Figure 1, with a notable increase of incidence starting from 2000, and with boys being affected more than girls.

Anthropometrics

Forty-seven (81%) of the patients were African Americans, 8 (14%) were Arabic, 2 (3%) were Hispanic, and 1 (2%) was Caucasian. Among those with known religious preference, 19% were Muslims and 33% were Christians. Only 2 patients had information on sun exposure, and in both cases sun exposure was limited. Data on patients' use of sunblock were not available.

Clinical Presentation and Course

Most of the cases were seen during winter (18, or 31%), spring (18, or 31%], and fall (14, or 24%), but there were still quite a number (14%) of patients seen during the summer months. Twelve (21%) were seen at the outpatient clinic and 46 (79%) at the ED, of which 33 (57%) were hospitalized. Common clinical manifestations are shown in Table 1, with joint swelling, rachitic rosary, and bowing of legs

Table 1. Common Manifestations of Rickets in Children's Hospital of Michigan

Presentation	No. of Cases	Percentage
Symptoms		
Wide swollen joints	34/46	74
Rachitic rosary	25/39	64
Bow legs	22/38	58
Bone pains	10/28	36
Frontal bossing	13/36	36
Fracture	9/36	25
Motor delay	8/26	31
Seizures	7/23	30
Neuroirritability	7/23	21
Apnea	2/15	13
Wobbly/wide-based gait	2/36	5
Large anterior fontanel	2/36	5
Delayed dentition	1/36	3
Knock knee	1/36	3
Laboratory findings		
Low calcium	27/47	57
Low phosphate	24/47	52
Increased alkaline phosphatase	46/47	98
Low 25-OH vitamin D	37/47	79

being the most identifiable abnormalities. On growth profile, 17 (47%), 15 (31%), and 4 (29%) patients with nutritional rickets were below the fifth percentile for height, weight, and head circumference, respectively.

Rickets was diagnosed incidentally in 26 (45%) of the cases, and of these cases, 22 were diagnosed in the ED while the patients were being evaluated for other problems such as wheezing, fever, failure to thrive, diarrhea, and fractures. Thirty-two (55%) of the cases were either known cases of rickets or primarily presented (11 cases) with symptoms and signs of rickets. Reasons for admission were seizures (7 patients), carpopedal spasm (1 patient), and referrals from other institutions for management of severe hypocalcemia (3 patients).

Nutrition History

Among the 49 cases, 47 (96%) were exclusively breast-fed from 4 to 18 months of age, and 2 (4%) patients were both formula-fed and breast-fed. Information on the quantity of cow milk formula given per day to both infants was not available. Duration of breast-feeding was between 2 and 19 months, with a mean of 9.55 months. At the time of diagnosis, 30 (61%) patients were still breast-fed and also received table foods, whereas 11 (23%) were fed with baby foods or table foods and did not receive milk or milk alternatives, and 8 (16%) were weaned to non–cow's milk formula (eg, soy, goat milk). Among the 11 patients who did not receive milk supplements, 7 (64%) were given cheese or yogurt as a calcium source. Unfortunately, data were not available regarding quantity of food intake. Of the 40 patients who were asked about vitamin supplements, only 7 (18%) had received multivitamins. All these 7 patients were already diagnosed with or suspected of having rickets and were started on multivitamins by the primary care physicians.

Laboratory Findings

Calcium levels were low in 57% and normal in 43% of the cases, and phosphate levels were low in 52% and normal in 48% of cases, whereas alkaline phosphatase was elevated in 98% of cases. Hemoglobin and hematocrit were normal in 71% (34 of 48) and 75% (36 of 48) of the patients. 25-OH vitamin D [25(OH) D] was low (<20 ng/mL) in 79% (33 of 48) and normal (≥20 ng/mL) in 21% (9 of 42) of the patients. Of those patients with low levels of 25(OH) D, 42% (14 of 33) were below detectable levels of less than 5 ng/mL, all were African Americans, and 57% (8 of 14) presented in spring. Among these patients with undetectable 25(OH) D levels, only 1 was Muslim; in 50% (7 of 14) of the patients, religion was not documented, and the rest were Christians. 1,25-dihydroxy vitamin D [1, 25(OH) D] was normal in 55% (17 of 31), elevated in 39% (12 of 31), and low in 6% (2 of 31) of the cases. Parathyroid hormone was high in 87% (27 of 31) and normal in 13% (4 of 31) of the patients. X rays showed changes associated with rickets in 96% (53 of 55) and osteopenia in 2% (1 of 55) of the patients; 2% (1 of 55) of the patients had normal X rays.

Treatment

After the diagnosis was established, the patients were treated with ergocalciferol orally or intramuscularly (including stoss therapy) and with calcium orally or intravenously.

Follow-up

Twenty-five (43%) of the patients were followed at Children's Hospital of Michigan. Sixteen of those

patients were eventually lost to follow-up, and therefore we could document resolution of rickets in only 8 patients. Follow-up ranged from 1 week to 36 months, with a mean of 6.6 months. During follow-up, serum levels of calcium and phosphorus levels were normal in 92% and 100% of the patients, respectively, whereas alkaline phosphatase continued to be elevated in 62% of the patients. Of those 8 patients considered to have had complete resolution of rickets, 1 had persistent bowing of legs and was referred to orthopedics. Two patients who eventually lost to follow-up still showed bowing of legs at 2 to 3 months follow-up, and 1 patient continued to have widened wrists and remnants of rachitic rosary with myopathy of legs for 10 months. These 3 patients had an initial 25(OH) D level of less than 5 ng/mL.

Repeat radiological studies were performed on 17 patients from 1 week to 30 months after diagnosis and initiation of treatment. Eleven (65%) patients showed evidence of healing rickets, and complete or near complete resolution was seen in 5 patients.

Discussion

Nutritional rickets is most commonly caused by vitamin D deficiency, but it can also be caused by deficiency of calcium or deficiency of both calcium and vitamin D. Unfortunately, rickets is on the rise today and is a widespread public health concern.[7] This rise in rickets could be the result of decreasing sunlight exposure, an increasing number of women who are breast-feeding, or increasing maternal vitamin D deficiency.[7,8] It is also worth noting that there is a decline in the number of pediatricians who recommend vitamin D supplementation for breast-fed infants.[9] In addition, rebound of rickets can be caused by the use of sunscreen and the avoidance of direct sunlight because of the risk for melanoma. Although most experts agree that sensible sun exposure is an important modality in the prevention of vitamin D deficiency, it is still a controversial issue.[10] Other contributing factors to the rebound of nutritional rickets can include resistance to supplementation on the part of lactation consultants (see information on the Le Leche League International Web sites)[11] and the inconsistencies of the recommendations of the American Academy of Pediatrics (AAP) over the years about vitamin D supplementation.[12-14] At present, the perceived physiologic level for serum 25(OH) D and dose for adequate intake of vitamin D for infants and pregnant women are also in question and under investigation.[15,16]

Similar to other studies,[8,16,17] there were significantly more males (62%) than females (38%) in our study. The age range was likewise similar to those in other reports,[8,16,18] although the oldest patient in our study was 11 years old. In addition, as reported by others,[8,18] African Americans accounted for most (87%) of the ethnic groups affected. Significantly, the Arabic community came in second, and among identified religious practices, Muslims (19%) had the largest number of cases. Unfortunately, no information was available on the practices of these Muslim patients (eg, covering the entire body, etc). In the 2 cases in which information on sun exposure was available, the patients were both Muslims and wore burkas. In 1985, Specker et al[19] declared sunshine exposure to be a relevant source for 25(OH) D in exclusively breast-fed infants regardless of maternal 25(OH) D status. Any blockage of the penetration of ultraviolet B photons (290–315 nm), which occurs in deeply pigmented skin,[20] with the use of sunscreen,[21] with full body covering,[22,23] and at latitudes above 35°—especially during the winter months[24,25]—significantly decreases vitamin D_3 production. Webb[24] reported that previtamin D production was significantly low to almost none in Boston, Massachusetts (42°N), and Edmonton, Canada (52°N), during the winter months. Michigan is at 41° to 48° N latitude, and in Detroit, sunshine on average can be seen on only 32% of the days in December and January and on only 49% of the days year round.[26] This explains why rickets was seen all throughout the year in Detroit, with most of the cases occurring during winter and spring.

As reported by others,[8,17] 96% of our patients were exclusively breast-fed for 4 to 18 months. In 2 patients, parents reported using formula in addition to breast-feeding. It is possible that the amount of formula fed to these patients may have been insufficient to provide enough vitamin D. Breast milk contains 15 to 50 U/L of vitamin D,[27,28] which is significantly below the recent recommendation of 200 U/day made by the National Academy of Sciences.[29] In 1963, the AAP Committee on Nutrition recommended that all infants and children receive 400 U of vitamin D as

early as the first 2 weeks of life[12]; this recommendation was modified in 1978.[13] The 1998 *Pediatric Nutrition Handbook* recommended 400 U of vitamin D for breast-fed infants but limited this recommendation to dark-skinned babies.[29] In 2003, because of continued reports of rickets, the AAP released a new guideline suggesting a minimum of 200 U/day of vitamin D for all infants exclusively breast-fed and for those consuming less than 500 mL of milk formula daily.[14] Hopefully, this change will help prevent nutritional rickets in exclusively breast-fed infants. Recent studies revealed that giving mothers higher doses (>1000 U) of vitamin D supplementation during pregnancy and lactation had substantial improvement on 25(OH) D status in both nursing infants and lactating mothers.[30,31]

Rickets is frequently missed in primary care clinics.[32] In this study, in both ED and clinic settings, about half the patients were diagnosed with rickets incidentally. Clinical presentation, biochemical abnormalities, and radiological findings of nutritional rickets were similar to those reported in other studies.[8,16,33,34] Wide, swollen joints; rachitic rosary; and bowed legs were the most identifiable abnormalities. Malnutrition was likewise a prominent component during presentation.[8,16]

In spite of the renewed AAP recommendation on vitamin D supplementation in 2003, none of our patients received vitamin D supplementation, and there was also a notable, consistent increase in the cases of nutritional rickets observed, starting in 2000. One of the reasons could be the increase in breast-feeding rates. In 2004, the Michigan Surgeon General's health status report on Michigan Health 2010 noted steadily increasing breast-feeding rates since 1991 (48.8%), rising to an all-time high of 64.3% in 2001, which was comparable to 69.5% nationwide.[30] The report stated that the 6-month breast-feeding rate in the state of Michigan likewise increased from 15.9% in 1991 to 26.5% in 2001. Breast-feeding in the state of Michigan is reportedly practiced most among Hispanics and least in African Americans, at 65.3% and 32.6%, respectively.[35] The population breakdown of the Detroit community[36] is predominantly African Americans at 81%, followed by 8% Caucasians; 5% Hispanics; 5% other ethnic groups, such as Arabic; and 1% Asian/Pacific Islanders. Despite the low breast-feeding rates in African Americans, the actual number of infants who are breast-fed is relatively high compared with other ethnic groups. Another factor that could have contributed to the increase in the cases of rickets is the increasing number of patients seen at our institution.

Skeletal muscle possesses vitamin D receptors, and muscle function needs 1,25(OH) D. Therefore, patients with rickets may have severe muscle weakness, decreased muscle tone, and flabby legs.[28] Three of our patients who showed poor healing after treatment had initial 25(OH) D levels below 5 ng/mL.

To solve the problem of follow-up and failure of secondary prevention, a single-day inpatient therapy has been suggested. In our institute, stoss therapy was the preferred treatment, but it had to be discontinued because of the unavailability of the depot vitamin D preparation.

There are several limitations in this study. Information on sun exposure, use of sunblock, patients' diet, and maternal intake of vitamin D during pregnancy and lactation was incomplete. The accuracy of the information, especially with regard to diet, is subject to recall bias. Records on breast-feeding at Women, Infants, and Children were likewise limited.

In summary, there has been an increase in the number of rickets cases since 2000 that could be related to the rising breast-feeding rates and number of patients seen at our institution. Most of the cases were African Americans, Arabic, and Muslims. The patients were exclusively breast-fed without multivitamin supplements. Almost a fourth of the cases were weaned from breast-feeding and the subsequent diet did not include milk or milk alternatives. Seventy-nine percent of the patients presented at the ED, and rickets was an incidental finding in 69% of those patients. Our goal as pediatricians should be to make sure all infants are vitamin D sufficient.

References

1. Hypponen E, Laara E, Jarvelin M-R, Virtanen SM. Intake of vitamin D and risk of type 1 diabetes: a birth-cohort study. *Lancet*. 2001;358:1500-1503.
2. Bischoff-Ferrari HA, Borchers M, Gudat F, Durmuller U, Stahelin HB, Dick W. Vitamin D receptor expression in human muscle tissue decreases with age. *J Bone Miner Res*. 2004;19:265-269.
3. Chen TC, Holick MF. Vitamin D and prostate cancer prevention and treatment. *Trends Endocrinol Metabol*. 2003;14:423-430.

4. Khatib R, Alsaek Y, Çakan N, Kamat D. Nutritional rickets. *Consultant Pediatricians*. 2005;4:33-39.
5. Khatib R, Çakan N, Kamat D. X-linked hypophosphatemic rickets. *Consultant Pediatricians*. 2007;6:77-84.
6. Kruger D, Lyne ED, Kleerekoper M. Vitamin D deficiency rickets. A report on three cases. *Clin Orthop*. 1987;224:277-283.
7. Weisberg P, Scanlon KS, Li R, Cogswell ME. Nutritional rickets among children in the United States: review of cases reported between 1986 and 2003. *Am J Clin Nutr*. 2004;80(6):1697S-1705S.
8. Carvalho N, Kennedy RD, Carrington PH, Hall DE. Severe nutritional deficiencies in toddlers resulting from health food milk alternatives. *Pediatrics*. 2001;107(4):E46.
9. Davenport ML, Uckun A, Calikoglu AS. Pediatrician patterns of prescribing vitamin supplementation for infants: do they contribute to rickets? *Pediatrics*. 2004;113(1):179-180.
10. Holick MF. Sunlight and vitamin D for bone health and prevention of autoimmune diseases, cancers, and cardiovascular disease. *Am J Clin Nutr*. 2004;80(suppl): 1678S-1688S.
11. Mojab CG. Sunlight deficiency and breastfeeding. *Breastfeeding Abstr*. 2002;22:3-4.
12. American Academy of Pediatrics, Committee on Nutrition. The prophylactic requirement and the toxicity of vitamin D. *Pediatrics*. 1963;31:512-525.
13. American Academy of Pediatrics, Committee on Nutrition, Nutrition Committee of the Canadian Pediatric Society. Breast-feeding. *Pediatrics*. 1978;62:591-601.
14. American Academy of Pediatrics, Committee on Nutrition, Section of Breast Feeding Medicine. Prevention of rickets and vitamin D deficiency: new guidelines for vitamin D intake. *Pediatrics*. 2003;111:908-910.
15. Pettifor J. The epidemiology of vitamin D and calcium deficiency. In: Pettifor J, Zlotkin, S, eds. *Micronutrient Deficiencies During the Weaning Period and the First Years of Life*. Sao Paulo: Nestec; 2004:21-35.
16. From the Centers for Disease Control and Prevention. Severe malnutrition among young children—Georgia, January 1997-June 1999. *JAMA*. 2001;285(20):2573-2574.
17. Cosgrove L, Dietrich A. Nutritional rickets in breast-fed infants. *J Fam Prac*. 1985;21(3):205-209.
18. Kreiter S, Schwartz RP, Kirkman HN, Charlton PA, Calikoglu AS, Davenport ML. Nutritional rickets in African American breast-fed infants. *J Pediatr*. 2000; 137(2):153-157.
19. Specker B, Valanis, B, Hertzberg, V, Edwards, N, Tsang, RC. Sunshine exposure and serum 25-hydroxyvitamin D concentrations in exclusively breast-fed infants. *J Pediatr*. 1985;107(3):372-376.
20. Clemens T, Adams JS, Henderson SL, Holick MF. Increased skin pigment reduces the capacity of skin to synthesize vitamin D3. *Lancet*. 1982;1(8263):74-76.
21. Matsuoka L, Ide L, Wortsman J, MacLaughlin JA, Holick MF. Sunscreens suppress cutaneous vitamin D3 synthesis. *J Clin Endocrinol Metabol*. 1987;64(6): 1165-1168.
22. Salih F. Effect of clothing varieties on solar photosynthesis of previtamin D3: an in vitro study. *Photodermatol Photoimmunol Photomed*. 2004;20(1):53-58.
23. Matsuoka L, Wortsman J, Dannenberg MJ, Hollis BW, Lu Z, Holick MF. Clothing prevents ultraviolet-B radiation-dependent photosynthesis of vitamin D3. *J Clin Endocrinol Metabol*. 1992;75(4):1099-1103.
24. Webb A, 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 Metabol*. 1988;67(22):373-38.
25. Holick M. Environmental factors that influence the cutaneous production of vitamin D. *Am J Clin Nutr*. 1995;61(3):638S-645S.
26. City-data.com. Michigan—location, size, and extent, topography, climate, flora and fauna. http://www.city-data.com/states/Michigan.html. Accessed November 13, 2007.
27. Reeve L, Chesney RW, Deluca HF. Vitamin D of human milk: identification of biologically active forms. *Am J Clin Nutr*. 1982;36(1):122-126.
28. Leerbeck E, Sondergaard H. The total content of vitamin D in human milk and cow's milk. *Br J Nutr*. 1980; 44(1):7-12.
29. Institute of Medicine, Food and Nutrition Board, Standing Committee on the Scientific Evaluation of Dietary Reference Intakes. Vitamin D. In: *Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride*. Washington, DC: National Academy Press; 1997:250–287.
30. Ala-Houhala M, Koskinen T, Terho A, Koivula T, Visakorpi J. Maternal compared with infant vitamin D supplementation. *Arch Dis Child*. 1986;61(12): 1159-1163.
31. Hollis B, Wagner CL. Assessment of dietary vitamin D requirements during pregnancy and lactation. *Am J Clin Nutr*. 2004;79(5):717-726.
32. Rudolf M, Arulanantham K, Greenstein RM. Unsuspected nutritional rickets. *Pediatrics*. 1980;66(1):72-76.
33. Tomashek K, Nesby S, Scanlon KS, et al. Nutritional rickets in Georgia. *Pediatrics*. 2001;107(4):E45.
34. Holick M. Resurrection of vitamin D deficiency and rickets. *J Clin Invest*. 2006;116(8):2062-2072.
35. Wisdom K, Olszewski J. Michigan Surgeon General's Health Status Report: Healthy Michigan 2010. http://www.michigan.gov/documents/Healthy_Michigan_2010_1_88117_7.pdf. Accessed November 13, 2007.
36. US Census Bureau. Detroit (city) QuickFacts from the US Census Bureau. http://quickfacts.census.gov/qfd/states/26/2622000.html. Accessed November 13, 2007.