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EDITORIAL

Vitamin D insufficiency/deficiency – a conundrum

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In this issue of the journal, Drs. Kathy Keller and Patrick Barnes present a commentary on the nutritional state of children in different parts of the world. For radiologists, the vitamin D insufficiency/deficiency pandemic might come as a surprise; however, as Keller and Barnes point out, the actual vitamin D level in children throughout the world is both a nutritional and a cultural problem and is quite well reported: "... 52% of Hispanic and black adolescents in a study in Boston and 48% of white preadolescent girls in a study in Maine had 25-hydroxyvitamin D levels below 20 ng per milliliter" [1–3]. The accepted level for deficiency of vitamin D is less than 20 ng/ml and of insufficiency is less than 30 ng/ml. Holick's article [1] is quite informative and worth reading in its entirety. However, Keller and Barnes do not stop at informing us about this deficiency but go on to postulate that the lack of vitamin D in some children is responsible for skeletal lesions that are characteristic of child abuse. In a related commentary, Dr. Russell Chesney [4], noted nephrologist and chairman of the Department of Pediatrics at the University of Tennessee Health Science Center, helps us understand the pediatric view on both issues. A third commentary by Dr. Carole Jenny [5], head of the American Academy of Pediatrics Section on Child Abuse, discusses why the vitamin D problem and child abuse are clearly two separate entities and when they are, in fact, related and when they are not.

Have Keller and Barnes taken two separate entities and tried to connect them? Are they related, or is there another answer?

We believe that it is one of the responsibilities of a medical journal to publish articles that present data that force us to rethink our preconceived notions. We believe it is important that all pediatric radiologists understand this issue, as we play a focal role in the diagnosis of child abuse. We want our readership to digest these commentaries before reading the last commentary in this issue – the editors' point of view [6]. We would then like you to draw your own conclusions about this current conundrum.

Editor's note: See related articles in this issue: Keller KA, Barnes PD doi:10.1007/s00247-008-1001-z; Chesney RW doi:10.1007/s00247-008-0993-8; Jenny C doi:10.1007/s00247-008-0995-6; Slovis TL, Chapman S doi:10.1007/s00247-008-0994-7.

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References

1. Holick MF (2007) Vitamin D deficiency. N Engl J Med 357:266–281
2. Gordon CM, DePeter KC, Feldman HA et al (2004) Prevalence of vitamin D deficiency among healthy adolescents. Arch Pediatr Adolesc Med 158:531–537
3. Sullivan SS, Rosen CJ, Halteman WA et al (2005) Adolescent girls in Maine at risk for vitamin D insufficiency. J Am Diet Assoc 105:971–974
4. Chesney RW (2008) Rickets or abuse, or both? Pediatr Radiol. doi:10.1007/s00247-008-0993-8
5. Jenny C (2008) Rickets or abuse? Pediatr Radiol. doi:10.1007/s00247-008-0995-6
6. Slovis TL, Chapman S, (2008) Evaluating the data concerning vitamin D insufficiency/deficiency and child abuse. Pediatr Radiol. doi:10.1007/s00247-008-0994-7

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COMMENTARY

Rickets or abuse, or both?

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Pediatric radiologists are often the first physicians to make the diagnosis of either rickets or child abuse in infants and young children. In a busy pediatric radiology department, these diagnoses are not rare, and appear to be increasing in frequency [1, 2]. At least three issues are not always clear. First, the laboratory values of serum calcium, phosphate and alkaline phosphatase activity are broadly ranging in infants and children [3]. Hence, in an individual patient, the biochemical evidence of vitamin D-deficiency rickets can be problematic. Second, patients with metaphyseal lesions and/or rib fractures are sometimes said to have "pathognomonic findings" of either rickets or abuse [2, 4]. Fractures at these locations are found in a wide variety of inherited and metabolic disorders as well as in cases of trauma [5]. Third, these two conditions are sometimes found together, which I have personally seen.

The pathologic lesions in bone of a rachitic child include soft ribs, an enlarged costochondral junction, and irregularly thickened growth plates of long bones [4]. Histologically, islands of hypertrophic cartilage are evident within the metaphyseal trabeculae. The thickened, irregular trabeculae are often lined by wide osteoid seams. These findings account for the widening of the spaces between the physes and for fraying [4]. The pediatric radiologist must also be familiar with the constellation of skeletal findings in non-accidental trauma [2].

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We are in the midst of an epidemic of nutritional vitamin D-deficiency rickets that has been termed "the third wave of rickets" [6, 7]. The massive epidemic of rickets that occurred during the industrial revolution in northern cities in Asia, Europe and North America formed the first wave. It was due to the blocking of cutaneous ultraviolet irradiation by blackened skies due to universal coal burning. In this first wave, vitamin D deficiency with clinical evidence of rickets was found to affect up to 40–50% of children in various northern regions. The addition of irradiated ergosterol at 400 IU (a dose equivalent to 10 μg of vitamin D_2) to dairy products in the United States diminished the occurrence of rickets to the point that it became a curiosity [7]. Ironically, this quantity of vitamin D_2 was equal to that found in a teaspoonful of cod liver oil, a German remedy for rickets since the mid- to late 19th century [6, 7].

Factors contributing to the second wave were the universal use of breast milk by dark-skinned adherents of sects or religions that insisted that mothers wear covering robes and headdresses, which greatly limited sunlight exposure. Many of these individuals were Asians (Turks emigrating to Sweden or Germany and Indians to the United Kingdom), who moved to northern latitudes, and African-Americans living in northern United States cities [8]. This was a phenomenon of the 1980s. Pediatricians were reminded that human milk contained a suboptimal amount of vitamin D, and there were strong recommendations to supplement breast-fed infants with oral vitamin D [9].

The third wave has occurred since the mid-1990s and is largely found in breast-fed infants whose mothers are dark-skinned and remain indoors. This wave of rickets is very common in Canada, as well [10]. The finding of classic nutritional rickets in many infants has stimulated debate, and new American Academy of Pediatrics guidelines emphasize that all breast-fed American infants should receive an oral supplement of at least 200 IU (5 μg) of

vitamin D daily. The recommendation for Canadian infants is 400 IU [10, 11].

Inherent in each wave is that infants with rickets are born to mothers who are deficient or insufficient in vitamin D themselves [12]. Historically, several clinical factors combine to produce maternal vitamin D deficiency. During periods of industrialization, the smog of atmospheric particles from coal burning effectively blocked out ultraviolet light at the 288 nm wavelength necessary for vitamin D production. Many breast-feeding mothers are dark-skinned and wear robes or headdresses, such that the photocutaneous synthesis of vitamin D_3 from 7-dehydrocholesterol in skin cells is minimal or does not take place [8]. Currently, working mothers remain inside because of their jobs and the use of computers, and rarely go outside at a time of day when the incident angle of the sun is optimal for promotion of photocutaneous synthesis of the vitamin [13, 14]. Each of these factors can create a situation in which a woman who is vitamin D-deficient during pregnancy cannot transfer adequate stores of this prohormone to her fetus. Even with recommended doses of vitamin D in prenatal vitamins, this maternal vitamin D deficiency can be difficult to overcome [1].

The two forms of vitamin D—ergocalciferol, or vitamin D_2, and cholecalciferol, or vitamin D_3—are biologically equivalent in terms of healing rickets, but are derived from either dietary sources or supplements (D_2) or from sunlight (D_3). Each form of the vitamin must undergo further metabolic steps to produce the active hormone, 1,25 dihydroxyvitamin D [1]. This hormone enhances intestinal calcium and phosphate absorption from the gut. The importance of adequate circulating values of $1,25(OH)_2D$ is that it optimizes blood concentrations of calcium and phosphate, which allow mineralization of osteoid and suppression of excess parathyroid hormone synthesis and secretion. Since the zone of provisional calcification (mineralization) is between the metaphysis and the epiphysis, the infant or child with rickets has hypomineralization at the growth plate, producing the classic lesion of rickets. These undermineralized bones are soft ("osteomalacia"), can bend or bow and widen upon weight-bearing and are more liable to fracture [5].

A full and exhaustive discussion of metaphyseal lesions is beyond the scope of this article, but they are found both in rickets and in nonaccidental trauma [2, 13]. Of interest, metaphyseal lesions and fractures due to rough play or falls are found in the animal kingdom and have been reported recently in arctic foxes, alpacas, yearling steers and polar bear cubs [15–18].

The article by Keller and Barnes is highly informative with regard to the confusion concerning metaphyseal lesions in infants where abuse is considered. This paper points out how the differences between rickets and abuse are blurred. A partnership with the pediatrician is essential [19]. The child's history and environment are important. Historical information concerning feeding and sun exposure is also relevant. Laboratory studies in the child, including serum calcium and phosphate levels, and 25 hydroxyvitamin D and parathyroid hormone concentrations are indicated. Unfortunately, serum alkaline phosphatase activity is elevated both in rickets and in healing fractures. In the milieu surrounding suspected abuse cases, the full history can be difficult to obtain [19]. All of these factors are important to the radiologist when confronted with this scenario.

References

1. Holick MF (2007) Vitamin D deficiency. N Engl J Med 357:266–281
2. Kleinman PK, Marks SC, Blackbourne B (1986) The metaphyseal lesion in abused infants: a radiologic-histopathologic study. AJR 146:895–905
3. Robertson J, Shilkofski N (eds) (2005) The Harriet Lane handbook. Elsevier Mosby, Philadelphia
4. Rossier A, Arvay N, Blanchet G et al (1963) Fractures in rachitic children. J Radiol Electrol Med Nucl 44:377–378
5. Chesney RW (2007) Metabolic bone disease. In: Behrman R, Kliegman RM, Jenson HB et al (eds) Nelson textbook of pediatrics. Saunders, Philadelphia, p 2893
6. Chesney RW (2002) Rickets: the third wave. Clin Pediatr (Phila) 41:137–139
7. Holick MF (2006) High prevalence of vitamin D inadequacy and implications for health. Mayo Clin Proc 81:353–373
8. Bachrach S, Fisher J, Parks JS (1979) An outbreak of vitamin D deficiency rickets in a susceptible population. Pediatrics 64:871–877
9. Finberg L (1981) Human milk feeding and vitamin D supplementation – 1981. J Pediatr 99:228–229
10. Ward LM, Gaboury I, Ladhani M et al (2007) Vitamin D-deficiency rickets among children in Canada. CMAJ 177:161–166
11. Gartner LM, Greer FR (2003) Prevention of rickets and vitamin D deficiency: new guidelines for vitamin D intake. Pediatrics 111: 908–910
12. Bezerra FF, Cabello GM, Mendonca LM et al (2008) Bone mass and breast milk calcium concentration are associated with vitamin D receptor gene polymorphisms in adolescent mothers. J Nutr 138:277–281
13. Kleinman PK, Marks SC Jr (1996) A regional approach to classic metaphyseal lesions in abused infants: the distal tibia. AJR 166:1207–1212
14. Pugliese MT, Blumberg DL, Hludzinski J et al (1998) Nutritional rickets in suburbia. J Am Coll Nutr 17:637–641
15. Conlogue GJ, Foreyt WJ, Hanson AL et al (1979) Juvenile rickets and hyperparathyroidism in the Arctic fox. J Wildl Dis 15: 563–567
16. Hedberg GE, Dunker F, Chesney RW (2007) Pathogenesis of metabolic bone disease in captive polar bears (*Ursus maritimus*). Polar Bears International, Sebastopol, CA. http://www.polarbearsinternational.org/pbhc/hedberg.htm. Accessed 28 Aug 2008
17. Hill FI, Thompson KG, Grace ND (1994) Rickets in alpacas (Lama pacos) in New Zealand. N Z Vet J 42:229–232
18. Thompson KG, Cook TG (1987) Rickets in yearling steers wintered on a swede (Brassica napus) crop. N Z Vet J 35:11–13
19. Jenny C (2006) Evaluating infants and young children with multiple fractures. Pediatrics 118:1299–1303

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COMMENTARY

Rickets or abuse?

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An article in this month's journal presents a thorough review of the long-recognized problem of vitamin D deficiency in pregnant women and young children. The authors then present several cases of infants with multiple bony lesions. In the case presentations they imply that these children were suffering from vitamin D deficiency rickets, although the diagnosis of rickets apparently was not made in any of the children.

The source of the cases was not mentioned in the article, although I suspect that these may have been cases sent to an expert by attorneys. With the exception of case 5, it also was not stated in the article if the children were diagnosed as having been abused.

The problem with such a series of cases is that it might leave the impression that children with metaphyseal lesions and fractures are likely to have vitamin D deficiency rickets. A "convenience sample" can be misleading because it exhibits the logic error embodied by the *availability heuristic* [1]. Our perception of the frequency of events can be skewed by the examples available to the observer. It is difficult to make generalizations from a series of extreme cases. A person looking down from an airplane at the tops of mountains poking through the clouds who never sees the valleys between them cannot describe the terrain in a meaningful way. The reporting of cases collected from a forensic practice (if this is, in fact, the case) might lead to a biased sample rather than a statistically valid sample. In my practice, a child protection program in a northern climate that evaluates over 1,800 children per year for alleged abuse or neglect, we have been checking every child with multiple fractures for metabolic bone diseases for several years and have not yet identified a single child with vitamin D deficiency. One of my colleagues, however, did find one child, a solely breast-fed 9-month-old with obviously demineralized bones.

Since I am not a radiologist, I cannot comment on the radiological interpretation of these cases. However, I would be quite surprised if some of these bony abnormalities were not related to maltreatment. It is unclear whether the authors of the paper are trying to redefine the previously described radiological characteristics of rickets. However, a careful correlation of radiographs and biochemical parameters in infants with proven vitamin D deficiency could be undertaken to examine the issue and address it as a valid research question. On the other hand, the careful clinical/pathological correlations of metaphyseal fractures that have been done by Dr. Paul Kleinman and his colleagues cannot be ignored and should continue to guide our practice until new discoveries are made using valid methodology [2–5].

Every case of multiple fractures or suspected child abuse should be carefully evaluated. The collaboration of pediatric radiologists and pediatricians is an important part of this evaluation. In the field of pediatrics, the development of the new subspecialty, Child Abuse Pediatrics, will set standards for pediatrics experts [6]. Three years of fellowship training (including research training), board examinations, and stringent professional standards for continuing education along with self and peer evaluation will certainly nurture experts in the field and promote excellence in clinical practice.

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References

1. Tversky A, Kahneman D (1982) Availability: a heuristic for judging frequency and probability. In: Kahneman D, Slovic P, Tversky A (eds) Judgment and uncertainty: heuristics and biases. Cambridge University Press, Cambridge, UK, pp 163–178
2. Kleinman PK, Marks SC Jr (1998) A regional approach to the classic metaphyseal lesion in abused infants: the distal femur. AJR 170:43–47
3. Kleinman PK, Marks SC Jr (1996) A regional approach to classic metaphyseal lesions in abused infants: the distal tibia. AJR 166:1207–1212
4. Kleinman PK, Marks SC Jr (1996) A regional approach to the classic metaphyseal lesion in abused infants: the proximal tibia. AJR 166:421–426
5. Kleinman PK, Marks SC, Blackbourne B (1986) The metaphyseal lesion in abused infants: a radiologic-histopathologic study. AJR 146:895–905
6. Block RW, Palusci VJ (2006) Child abuse pediatrics: a new pediatric subspecialty. J Pediatr 148:711–712

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COMMENTARY

Evaluating the data concerning vitamin D insufficiency/deficiency and child abuse

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There is absolutely no question that serum levels of vitamin D in children in sections of the population of the US, Canada and various parts of the world are lower than the accepted normal [1]. There are many reasons for this, and the American Academy of Pediatrics and others are addressing dosage requirement for basic supplementation of vitamin D [2, 3]. The connection, however, between vitamin D insufficiency/deficiency and fractures in children with otherwise normal radiographs is another issue. What is the evidence for fragility of bones in children with insufficient levels of vitamin D and even in those with deficiency levels if the radiographs are normal, that is, when there is no radiographic evidence of rickets?

The definition of rickets is "an interruption in the development and mineralization of the growth plate of bone, with radiographic abnormalities" [4]. Merely having insufficiency/deficiency of vitamin D levels in the blood *does not* constitute rickets. It is, therefore, incumbent to show radiographic changes in the 30–50% of infants and children with low vitamin D to claim that they have rickets.

What are the radiographic findings of rickets?

1. *Diminished bone mineralization.*

This is a difficult determination on plain radiographs except in the premature, very-low-birth-weight population. Our digital imaging makes it much more difficult to assess bone mineralization. Even further subjectivity goes into the face and skull evaluation in the neonate and young infant. Keller and Barnes [5] give one reference supporting the concept that the skull and facial bones have the earliest changes [6]. Let us look critically at this reference. There were a total of 25 patients said to have rickets although no data are given supporting this. Although 80% of their patients were said to have demineralization of the skull, there was no control group in that study to determine if they could, indeed, distinguish those patients from normal infants or show that "the best location to search for radiographic evidence of congenital rickets and nutritional rickets in infants less than 3 months of age is the cranium and facial bone" [5]. In the referenced article, only six patients were under 3 months of age. There is no mention of what, if any, other findings of rickets were present. Thus, a major point in the Keller and Barnes commentary in the diagnosis of radiographic findings of rickets is a very weakly supported one.

2. *Changes of growing bone found at the physis and metaphysis.*

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In growing patients, not sick prematures, these findings are most characteristic of rickets:

(a) Demineralization of the zone of provisional calcification. "The initial radiographic finding is rarefaction of the normally sharply defined zone of provisional calcification on the metaphyseal side of the growth plate so that the metaphyseal bone fades gradually into the lucent physeal and epiphyseal cartilage" [7].
(b) Metaphyseal cupping and fraying. The cartilage becomes disordered (from its normal columnar pattern) and the affected metaphysis becomes frayed and cupped. Because of the loss of mineralization in the zone of provisional calcification, the epiphysis and metaphysis are widely separated. This is the most valuable sign of rickets. If the metaphysis and epiphysis including the physeal lines appear normal, the patient does not have radiographic rickets (excluding prematures).

It is apparent in all the images of Keller and Barnes that the epiphysis and metaphysis are not separated and the physis is normal. There is no cupping and fraying. By definition, radiological rickets is *not* present in these images. Keller and Barnes cite cupping of the distal ulna metaphysis. This is well known to be a normal finding in young infants and *not* to be considered radiographic evidence of rickets when it is the *only* finding (no changes of the radius or changes at the knees) [8]. None of the infants described by Keller and Barnes as examples of "healing" have the expected pattern of mineralization of the zone of provisional calcification.

3. *Deformity from rickets (osteomalacia).*

Vertebral compression fractures have been described in rickets in children with seizures and severe rachitic bone diseases. However, there have not yet been any reports of isolated vertebral compression fractures in patients with proven rickets that were believed to be due to vitamin D insufficiency. Pending such reports, the claim of Keller and Barnes of such a mechanism is questioned. Therefore, *isolated* vertebral axial load compression fractures *are not and cannot be* the result of rickets, as Keller and Barnes claim. There is *no* literature to support these claims.

Congenital rickets

Let us examine "congenital rickets." Keller and Barnes refer to patients with congenital rickets (infants less than 6 months of age) as having "normal-appearing bone to diffuse cortical rarefaction, fractures at birth, and metaphyseal fraying and cupping" [5]. These patients appear in Table 1 [9–14]. Three of the seven infants were premature and one was near term. Three of the mothers had renal failure or severe preeclampsia. Two other mothers had hypocalcemia or diminished vitamin D. All of the infants had abnormal physical examinations and all who had radiographs (six of seven) had abnormal findings; there were metaphyseal changes in all six infants.

Thus, it is not reasonable to assume that an infant with shaft fractures or vertebral fractures and no metaphyseal changes has congenital rickets or, without appropriate biochemical parameters, rickets of any sort. One additional point made by these cases shows that the disturbed maternal calcium homeostasis with a low exchangeable pool in mothers with osteomalacia is as important as vitamin D levels in causing the baby's problem.

The occurrence of fractures secondary to a metabolic disease is complex. In "congenital rickets," it is the maternal calcium homeostasis that probably plays a major role. In a recent case-control study by Olney et al. [15], 68 children with two or more incidences of low-energy fractures were compared with a control group (57 children) without fractures. Their ages ranged from 3 to 18 years. A significant number of children with fractures and control subjects had idiopathic hypercalciuria based on 24-h urine collection. These children (in both groups) had lower bone density. Though both groups (21% of the children with fractures and 18% of the controls) had insufficient vitamin D levels, this was not a significant factor in those who had recurrent fractures.

Where are we now in trying to connect vitamin D deficiency rickets and child abuse? Let us look once more at the cases Keller and Barnes submitted:

1. The authors do not give us their selection criteria for the patients presented, i.e. exclusion criteria and total pool from which they were selected. It appears that the patients were selected from among those involved in litigation concerning whether child abuse was present.
2. None of the children had vitamin D levels reported at the time they were supposed to have rickets.
3. None of the children had calcium phosphate, alkaline phosphatase, or parathyroid hormone values reported at the time they were supposed to have rickets.
4. All of the children were below 4 months of age. All of the "congenital rickets" reports summarized in Table 1 had abnormal radiographs in a manner described above for rickets. Among the patients presented by Keller and Barnes, however, there was not one who had a widened physis or, on the recovery films, had the characteristic appearance of healing rickets.

Table 1 Findings of infants with congenital rickets.

Reference	No. of patients	Maternal history	Baby's maturity	Baby's clinical status	Radiographic findings (as stated in article)
9	1	Renal failure	27 weeks/830 g	Hyaline membrane disease	Metaphyseal changes
10	1	Low vitamin D, 7.1 ng/ml	Term/2.75 kg	Craniotabes	Suture widening; metaphyseal changes at wrist
11	1	Severe preeclampsia; normal vitamin D	29 weeks/684 g; small for gestational age; premature	Normal at birth; respiratory distress at 2 weeks; elevated alkaline phosphatase; low calcium; died at 65 days	Day 1: fraying of metaphysis
12	2 A B	Normal calcium (6.5 mg/dl), phosphorus (5.5 mg/dl), PTH 32 pg/ml	Full term/3 kg; 36 weeks/2.4 kg	Hypocalcemic seizures on day 7: elevated alkaline phosphatase (52 KA units/100 ml); aminoaciduria at 2 weeks: craniotabes; calcium 6.8 mg/dl, phosphorus 5.5 mg/dl, alkaline phosphatase 70 KA units/100 ml	No radiographs at time of illness. At 2 weeks: normal skull; long bones acute rickets
13	1	Hypocalcemia 4.3 mE/l	Full term/2.5 kg	Craniotabes; prominence of costochondral junctions and widening of wrists	Metaphyseal changes: wrists and lower limbs generalized rarefaction, cupping and fraying
14	1	Renal failure, polyhydramnios	31 weeks/1.12 kg	Tetany at 3 days; low serum calcium phosphate; high parathyroid hormone	Fracture femur; fracture ribs; rickets long bones

5. The fractures shown are mainly that — fractures. The areas in which one expects to see signs of rickets in this age group are all normal.
6. The normal variant of a mildly cupped ulna with a normal radius is normal, and therefore not an example of rickets [8].

Are any, some, or all of these children abused? Diminished fractures and healing would not be expected until treatment was initiated. Did further fractures occur after initiation of child protection procedures as might be expected if vitamin D deficiency was present? The radiographic and limited clinical data of the cases presented suggest that a child protection team (or equivalent) needs to investigate the possibility of child abuse while continuing to consider other causes of injury. How many of these children had retinal hemorrhages or external signs of trauma? Were the fractures multiple and/or occurring at different times? What was the social situation? Was there any history to support accidental injury? While there are no data, in our opinion, to suggest any of the lesions described by Keller and Barnes are rachitic, we must keep an open mind until a full work-up, as described by the American Academy of Pediatrics [16], is fulfilled. Kleinman [17, 18] has enlightened us on the nature of the classic metaphyseal lesion, and over 15% of his text concerns the differential diagnosis of this lesion and the work-up of those diseases that may masquerade as child abuse.

The diagnosis of child abuse is a team effort. One must consider the *entire* situation. The entire clinical, laboratory, radiographic, and, most importantly, social evaluation must be taken into consideration before reaching a conclusion.

A final word about the vitamin D pandemic — the *denominator* is crucial. If vitamin D insufficiency/deficiency is so prevalent and this causes weakened bones, where are the increased cases of bone changes and fractures consistent with rickets? In particular, where are the birth-related fractures? With the accounts recording the low maternal vitamin D level, one would expect a much larger number of fractures, many of which should be clinically apparent. Perhaps other factors are necessary (disordered maternal calcium metabolism, increased urinary excretion of calcium, etc.) and are equal in importance for bones to be weakened [15].

In the article by O'Connell and Donoghue [19] that provides Keller and Barnes a foundation for their commentary, there were three classic metaphyseal lesions per 187,000 births or an incidence of 0.0016%. We are not given the denominator that is the total number of cesarean sections [20] but, in fact, even if cesarean sections accounted for one-third to one-half of all the deliveries, the incidence of classic metaphyseal lesions would only increase to 0.0048%. Perhaps O'Connell and Donoghue missed a clue as to why these babies were injured, such as the delivery technique or some unusual handling of the baby after delivery. While we do not know what caused the

babies' problems precisely, these lesions as shown by O'Connell and Donoghue are extremely rare and do not force us to postulate underlying abnormal bone.

In conclusion, the demonstration of vitamin D insufficiency/deficiency levels and the bone changes of rickets are not the same. Each must be considered separately. For these reasons and because of the other data described, we find that the connection made by Keller and Barnes between "rickets" and fractures they consider to be similar in appearance to those seen in child abuse is not based on any scientific data. Unfortunately, the current scenario is reminiscent of Paterson's "temporary brittle bone disease" [21]. This concept has remained without proof and has been discredited [22–25]. The work-up of child abuse considers a differential diagnosis including rickets but, unless there is reasonable evidence of rachitic bone disease, there is no scientific basis for confusing vitamin D insufficiency/deficiency alone with child abuse.

References

1. Holick MF (2007) Vitamin D deficiency. New Engl J Med 357:266–281
2. Gartner LM, Greer FR; Section on Breastfeeding and Committee on Nutrition. American Academy of Pediatrics (2003) Prevention of rickets and vitamin D deficiency: new guidelines for vitamin D intake. Pediatrics 111:908–910
3. Roth DE, Martz P, Yeo R et al (2005) Are national vitamin D guidelines sufficient to maintain adequate blood levels in children. Can J Public Health 96:443–449
4. Dorland's illustrated medical dictionary, 30th edn (2003) Definition of rickets. Saunders, Philadelphia, p 1633
5. Keller KA, Barnes PD (2008) Imaging findings in congenital rickets. Pediatr Radiol 38 [Suppl 2]:S292–S293
6. Swischuk LE, Hayden CK Jr (1977) Seizures and demineralization of the skull. Pediatr Radiol 6:65–67
7. Shore RM (2008) Metabolic bone disease. In: Slovis TL (ed) Caffey's pediatric diagnostic imaging, 11th edn. Elsevier, Philadelphia, pp 2728–2732
8. Glaser K (1949) Double contour, cupping and spurring in roentgenograms of long bones in infants. Am J Roentgenol Radium Ther Nucl Med 61:482–492
9. Kirk J (1982) Congenital rickets -- a case report. Aust Paediatr J 18:291–293
10. Moncrieff M, Fadahunsi TO (1974) Congenital rickets due to maternal vitamin D deficiency. Arch Dis Child 49:810–811
11. Zeidan S, Bamford M (1984) Congenital rickets with maternal pre-eclampsia. J R Soc Med 77:426–427
12. Ford JA, Davidson DC, McIntosh WB et al (1973) Neonatal rickets in Asian immigrant population. BMJ 3:211–212
13. Mohapatra A, Sankaranarayanan K, Kadam SS et al (2003) Congenital rickets. J Trop Pediatr 49:126–127
14. Al-Senan K, Al-Alaiyan S, Al-Abbad A et al (2001) Congenital rickets secondary to untreated maternal renal failure. J Perinatol 21:473–475
15. Olney RC, Mazur JM, Pike LM et al (2008) Healthy children with frequent fractures: how much evaluation is needed. Pediatrics 121:890–897
16. Jenny C; Committee on Child Abuse and Neglect (2006) Evaluating infants and young children with multiple fractures. Pediatrics 118:1299–1303
17. Kleinman PK (1998) Diagnostic imaging of child abuse, 2nd edn. Mosby, St. Louis
18. Kleinman PK (2008) Problems in the diagnosis of metaphyseal fractures. Pediatr Radiol 38 [Suppl 3]:S388–S394
19. O'Connell AM, Donoghue VB (2007) Can classic metaphyseal lesions follow uncomplicated caesarean section? Pediatr Radiol 37:488–491
20. O'Connell AM, Donoghue VB (2008) Classic metaphyseal lesions follow uncomplicated caesarean section NOT brittle bone disease. Pediatr Radiol 38:600
21. Paterson CR (1990) Osteogenesis imperfecta and other bone disorders in the differential diagnosis of unexplained fractures. J R Soc Med 83:72–74
22. Chapman S, Hall CM (1997) Non-accidental injury or brittle bones. Pediatr Radiol 27:106–110
23. Ablin DS, Sane SM (1997) Non-accidental injury: confusion with temporary brittle bone disease and mild osteogenesis imperfecta. Pediatr Radiol 27:111–113
24. Mendelson KL (2005) Critical review of 'temporary brittle bone disease'. Pediatr Radiol 35:1036–1040
25. Bishop N, Sprigg A, Dalton A (2007) Unexplained fractures in infancy: looking for fragile bones. Arch Dis Child 92:251–256

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LETTER TO THE EDITOR

Reply regarding rickets vs. abuse: the evidence

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Editor's note: It is the policy of the journal to publish simultaneously, both online and in print, letters to the editor and the authors' reply. Because of the many revisions necessary before the authors' reply was accepted, Dr. Feldman's letter was mistakenly published online first. I apologize to Drs. Keller and Barnes for this inadvertent error in our editorial process. T.L. Slovis

Jenny [1], Chesney [2], Slovis and Chapman [3], and Feldman [4] seem to acknowledge the *evidence* that the highest rates of vitamin D deficiency (DD) are now being reported in undersupplemented breastfed infants younger than 6 months of age (including those born to mothers with DD). What is the *evidence* that DD can be congenital rickets? Greer [5] has concluded that "good evidence" exists that these infants are at *increased risk of rickets.* Jenny's article, referenced in Slovis and Chapman [3], on evaluating infants with multiple fractures states that a 25-OH-vitamin D level can be obtained "if rickets is suspected because of radiographic findings or *history.*" We agree with her call for a careful correlation of radiographs and biomechanical parameters in infant DD as a valid research project. Chesney [2] states that he has witnessed DD in an infant who was also "abused." This is not surprising since the age range of infant DD overlaps the peak age range for infant abuse [6]. In the face of this epidemic, why aren't there more reports of radiographic evidence of rickets in infants <6 months of age? Shouldn't these infants be at increased risk for fractures? Are there really no radiographic findings until the classic metaphyseal "cupping and fraying" occurs at 6 months or older? And do these classic changes develop so rapidly that no one has ever identified them in their earlier stages?

Yorifuji et al. [7], Gordon et al. [8], and Ward et al. [9] all report radiographic abnormalities of rickets in infants with DD but provide no illustrations. In his recent review, Kleinman et al. [10] lists *rickets* at the top of the differential diagnosis for the classic metaphyseal lesion (CML). He states, "on occasion discrete osseous fragments resembling corner fractures may be identified in the absence of more dramatic signs of rickets." Is he not describing the early signs of "CML-like lesions" in rickets? In both his book, as referenced in Slovis and Chapman [3], and his recent review [10], Kleinman clearly identifies rickets (along with other conditions) as a mimic of abuse, including the metaphyseal lesions, skull fractures, subperiosteal new bone formation, insufficiency fractures (e.g., Looser zones), and osteopenia.

In our case series, the radiologists originally described the bone findings as characteristic of abuse, often calling the bone mineralization normal, and provided no differential diagnosis to include bone fragility disorders. Yet, all these infants were asymptomatic and fit the classic demographic profile placing them in the highest-risk category for severe DD. This discrepancy between the radiographic findings and the clinical findings should not be ignored, particularly when the psychosocial evaluation of the caretaker shows no risk factors for abuse. Ruling out abnormal bone mineralization on radiography is

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unscientific and introduces bias. We must develop a better way of testing bone mineral density (BMD) for osteopenia and demineralization in these infants [11].

By radiography and CT, in our cases, we observed parasutural demineralization (i.e. pseudodiastasis), as previously described by Resnick [12] and Swischuk and Hayden [13], which correlates clinically with craniotabes. We also question that an imaging finding of persistent lückenschädel (lacunar skull change) in these infants may also indicate craniotabes. Slovis and Chapman focused on the lack of physeal widening, no cupping and fraying, the lack of radial involvement, and no classic findings of healed rickets in our cases. Establishing the separation of the epiphyses from the metaphyses on radiographs when the epiphyses are either not ossified or in the early stages of ossification has not been reported as far as we know [14]. The classic changes of cupping and fraying are usually not identified until 6 months or older [3, 14]. Swischuk and Hayden [15] and Silverman and Kuhn [16] noted the involvement of the distal ulna out of proportion to the radius. The healing pattern that has been "classically" described in *infantile* rickets occurs with vitamin D therapy *beyond* formula feeding or vitamin D supplementation [14]. Would we not expect a difference in the radiographic appearance of healing rickets treated with 2,000–6,000 IU per day as compared with 200–400 IU/day (see our infant cases 3, 4)? Slovis and Chapman agree that compression fractures occur in rickets but state that an isolated vertebral compression fracture cannot result from rickets due to vitamin D insufficiency. It should be realized that such a child may have previously been D-deficient. Furthermore, Slovis and Chapman do not address the other classic deformities of rickets that are present in our series, e.g., anterior ribs ("rachitic rosary"), "saber shin" deformity of the tibia, bowed limbs, and Looser zones. They also avoid the issues of pathologic fractures and pseudofractures, including CMLs and Looser zones.

Our point regarding the O'Connell and Donoghue [17] article on CMLs occurring in uncomplicated cesarean sections in the UK was not to show whether this occurs frequently but to acknowledge that these authors (along with Slovis/Chapman) seem to make the inference that the injury was inflicted by the medical staff. Perhaps we should also consider that there may have been a predisposition in these infants? This is especially a concern in the UK, where 18% of pregnant women have vitamin D levels <10 ng/ml [14].

The four cases in our rickets vs. abuse commentary indeed represent alleged child abuse cases that we reviewed on behalf of the defense. In addition to our institutional work as radiologic consultants in child protection cases, including prosecution cases, we also volunteer our services in defense cases, as many other child protection physicians do. This is in compliance with the AMA and ACR codes of ethics regarding medical expert testimony. In all four cases, no charges were submitted, but travel expenses were reimbursed (total $2,500 for all four cases). In three of the four cases, we did contact and consult with the treating radiologists. To comply with the journal format of *Pediatric Radiology*, our original text, figures, and references were substantially reduced. We listed in every case the number and type of fractures each infant was alleged to have, but our commentary was focused on the bone findings that should alert radiologists to the possibility of DD (alone or coexisting with abuse). Also, none of these infants had retinal hemorrhages. In all four cases, the *historical* data fulfilled the criteria for congenital rickets due to maternal-fetal and neonatal vitamin D deficiency plus radiographic findings previously published in the medical literature [14]. In all four cases, at presentation, infant vitamin D level determinations were recommended but not done.

Case 1 The clinical and radiographic information provided by Dr. Feldman for this case is incomplete. The diagnosis of abuse was initially made only from the radiographs. The forensic pediatrician recommended that no further bone fragility workup be performed. Social workers found absolutely no risk factors for abuse. The readers are invited to review Bodnar et al. articles [18, 19] and make their own judgment regarding misrepresentation of the literature. Dr. Feldman's comments regarding the literature about seasonal variations in maternal vitamin D levels must take into consideration sun exposure and dietary intake, both of which were deficient in this mother by *history*. Furthermore, both prenatal and neonatal vitamins have been shown to contain inadequate vitamin D. Dr. Feldman also misquotes the literature regarding vitamin D levels, including units of measurement, for both deficiency and insufficiency. The case was dismissed by the judge with the agreement of the attorney general.

Case 2 The judge ruled that the parents were responsible for the child's injuries. However, contrary to Dr. Feldman's account, the judge granted custody to the maternal grandparents, mandated further medical intervention for the child, and allowed parental visitation with the goal of eventual family reunification.

Case 3 Also contrary to Dr. Feldman's account, this case was dismissed including a full apology to the family from the state of jurisdiction.

Case 4 Dr. Feldman states that this infant had an "acute brainstem and cervical spinal cord injury," in addition to cervical vertebral and skull fractures. The infant also had extracerebral collections without signs of increased intracranial pressure or retinal hemorrhages. Dr. Feldman states that he published this case as an abusive cervical spinal

cord injury. In fact, on MRI the neuroradiologist was unable to date the injuries because they were not acute. Furthermore, the identification of a syrinx also indicated chronicity. The medical records showed that this infant was manually rotated during the delivery after the head had already presented. The head was twisted to bring the body into proper position for delivery. Maternal and infant vitamin D level determinations were not done. Despite the *history* of significant birth trauma, the judge found the parents responsible for the child's injuries.

In conclusion, we propose that: (1) Maternal-fetal and neonatal vitamin D deficiency (DD) exists and is increasing. (2) DD can produce imaging abnormalities prior to the classic changes of rickets and predispose the infant to "fractures." (3) The imaging findings of rickets are different in infants younger than 6 months of age compared to older infants. (4) These findings can mimic abuse (e.g., CMLs). (5) Infants with bone imaging findings suggestive of abuse should also have vitamin D level determinations. (6) Radiologists should provide a differential diagnosis when faced with bone imaging findings suggestive of abuse. (7) The significance of the imaging findings must always be considered in the context of the clinical, social, and biochemical aspects of the case. (8) It should be possible to collect reliable data (imaging findings, vitamin D levels, BMD) and test these hypotheses.

References

1. Jenny C (2008) Rickets or abuse? Pediatr Radiol 38:1219–1220
2. Chesney RW (2008) Rickets or abuse, or both? Pediatr Radiol 38:1217–1218
3. Slovis TL, Chapman S (2008) Evaluating the data concerning vitamin D insufficiency / deficiency and child abuse. Pediatr Radiol 38:1221–1224
4. Feldman K (2009) Commentary on "congenital rickets" article. Pediatr Radiol . doi:10.1007/s00247-009-1285-7
5. Greer FR (2008) 25-Hydroxyvitamin D: functional outcomes in infants and young children. Am J Clin Nutr 88:529S–533S
6. National Child Abuse and Neglect Data System (NCANDS) (2008) Nonfatal maltreatment of Infants. US Oct. 2005- Sep. 2006. CDC MMWR Report April 4. Available via www.cdc.gov/mmwr
7. Yorifuji J, Yorifuji T, Tachibana K et al (2008) Craniotabes in normal newborns: the earliest sign of subclinical vitamin D deficiency. J Clin Endocrinol Metab 93:1784–1788
8. Gordon CM, Feldman HA, Sinclair L et al (2008) Prevalence of vitamin D deficiency among healthy infants and toddlers. Arch Pediatr Adolesc Med 162:505–512
9. Ward LM, Gaboury I, Ladhani M et al (2007) Vitamin D deficiency rickets among children in Canada. CMAJ 177:161–166
10. Kleinman PK (2008) Problems in the diagnosis of metaphyseal fractures. Pediatr Radiol 38(Suppl 3):S388–S394
11. Kaste SC (2008) Bone Mineral Density Assessment (Chapter 169). In: Slovis TL et al (eds) Caffey's Pediatric Diagnostic Imaging (11th edn) Mosby Elsevier, Philadelphia, pp 2771–2775
12. Resnick D (1996) Bone and Joint Imaging, 2nd edn. Saunders, Philadelphia, pp 511–524
13. Swischuk LE, Hayden CK (1977) Seizures and demineralization of the skull. A diagnostic presentation of rickets. Pediatr Radiol 6:65–67
14. Keller KA, Barnes PD (2008) Rickets vs. abuse: a national and international epidemic. Pediatr Radiol 38:1210–1216
15. Swischuk LE, Hayden CK (1979) Rickets: a roentgenographic scheme for diagnosis. Pediatr Radiol 8:203–208
16. Silverman FS, Kuhn JP (1993) Caffey's Pediatric X-ray Diagnosis, 9th edn. Mosby, St. Louis, pp 1746–1751
17. O'Connell A, Donoghue V (2007) Can classic metaphyseal lesions follow uncomplicated caesarean section? Pediatr Radiol 37:488–491
18. Bodnar LM, Simhan HN, Powers RW et al (2007) High prevalence of vitamin D insufficiency in black and white pregnant women residing in the northern United States and their neonates. J Nutr 137:447–452
19. Bodnar LM, Catov JM, Roberts JM et al (2007) Prepregnancy obesity predicts poor vitamin D status in mothers and their neonates. J Nutr 137:2437–2442