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#### The Many Faces of Vitamin D Deficiency Rickets

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## The Many Faces of Vitamin D Deficiency Rickets

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#### **OBJECTIVES**

After completing this article, readers should be able to:

- **1.** Explain the relationship between breastfeeding and vitamin D deficiency.
- 2. List the clinical findings in rickets.
- **3.** Delineate the clinical finding that can direct physicians toward infants who are at highest risk for rickets.
- 4. Describe how to evaluate a child for and diagnose vitamin D deficiency rickets.
- 5. Delineate the management steps that can prevent the occurrence of rickets in children at risk.

#### Introduction

Contemporary physicians may think of vitamin D deficiency rickets as a disease of the past. In fact, it remains a significant cause of nutritional disease for infants as we enter the 21st century. Unlike iron deficiency anemia, there are no clear recommendations about whether or how to screen children for rickets. The following cases illustrate the many different presentations of rickets.

#### **Case Studies**

#### **PATIENT 1**

A 6-month-old African-American female developed cyanosis while breastfeeding followed by two tonic episodes consistent with infantile seizures. History revealed that she was breastfed exclusively, had received no vitamin D supplementation, and was receiving erythromycin for treatment of otitis media. Except for erythematous tympanic membranes, findings on physical examination were normal.

Laboratory studies (Table 1) demonstrated decreased serum calcium, elevated serum alkaline phosphate, decreased hydroxyvitamin D, and increased dihydroxyvitamin D. Serum creatinine and urea nitrogen values were normal. Radiography revealed osteopenic ribs and flared anterior aspects of the ribs. The distal radial and ulnar metaphyses were cup-shaped, and the distal femoral and proximal tibial metaphyses were slightly widened.

#### PATIENT 2

A 1-year-old African-American male presented with a 3-day history of cough, fever, and shortness of breath. Chest radiography revealed left pneumonia and a right-sided rib fracture. The infant had been breastfed without vitamin D supplementation.

Findings on physical examination included intercostal retractions, a temperature of  $38.7^{\circ}$ C (101.7°F), and a weight of 7.65 kg (<5th percentile). The rib insertion at the sternum was nodular.

Laboratory studies (Table 1) demonstrated decreased serum phosphorous, normal serum calcium, elevated serum alkaline phosphate, decreased hydroxyvitamin D, and increased dihydroxyvitamin D. Serum creatinine and urea nitrogen values were normal.

Skeletal radiographs revealed diffuse osteopenia, with flaring and irregularity of the distal metaphyses of all the long bones (Fig. 1). There was a fracture of the midshaft of the left femur with callous formation. Periosteal new bone formation was present along the shafts of the radii, ulnae, tibiae, and fibulae along with cortical irregularity of both fibulae and the left tibia. The anterior ends of the ribs were widened, and there was a displaced fracture of the posterior right seventh rib. There was a healing fracture of the right midclavicle. An infiltrate was noted in the hilum of the left lung.

A protective services investigation concluded that the history and fractures were consistent with the diagnosis of rickets.

#### PATIENT 3

The mother of an 18-month-old African-American boy expressed concern during a routine health supervision visit that her son had not begun to walk. He had been breastfed through 9 months of age and since weaning had received virtually no milk or vitamin D. His weight was 9.8 kg (<5th percentile), and he had bilateral wrist enlargement, lower limb bowing, and frontal bossing.

Laboratory studies (Table 1) demonstrated decreased phosphorus, decreased calcium, elevated alkaline phosphate, decreased hydroxyvitamin D, and increased dihydroxyvitamin D. Serum creatinine values were normal.

Radiographs showed severe osteopenia of the skeleton, with fraying and cupping of the metaphyses, especially in the wrists, and widening of the physes.

#### PATIENT 4

Lower limb bowing was noted during a health supervision visit in a 13-month-old African-American boy who had been primarily breastfed without vitamin D supplementation. He weighed 13.1 kg (>95th percentile), and his height was 83.9 cm (>95th percentile).

Laboratory studies (Table 1) demonstrated normal serum phosphorus and calcium, elevated serum alkaline phosphate, decreased serum hydroxyvitamin D, and increased serum dihydroxyvitamin D. Radiographs showed irregular fraying of the provisional zones of calcification in the distal femurs, radii, and ulnae.

#### CASE DISCUSSION

One primary care pediatrician diagnosed all of these patients within a

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TABLE 1. Summary of Serum Laboratory Results					
		PAT			
TEST	1	2	3	4	NORMAL RANGE
Calcium					
(mmol/L)	1.1	2.1	1.5	2.2	2.0 to 2.6 mmol/L
(mg/dL)	4.2	8.5	6.0	8.9	8.0 to 10.5 mg/dL
Phosphorus					-
(mmol/L)	1.6	0.6	0.8	1.4	0.9 to 1.6 mmol/L
(mg/dL)	6.2	2.3	3.0	5.4	3.5 to 6.2 mg/dL
Alkaline phosphatase					
(U/L)	702	443	3,244	924	150 to 420 U/L
Urea nitrogen					
(mmol/L)	< 0.4	1.1	N/A	N/A	1.8 to 8.9 mmol/L
(mg/dL)	<1.0	3.0	N/A	N/A	5.0 to 25.0 mg/dL
Creatinine					
(mcmol/L)	26.5	17.7	35.4	N/A	17.7 to 35.4 mcmol/L
(mg/dL)	0.3	0.2	0.4	N/A	0.2 to 0.4 mg/dL
25-OH vitamin D					
(nmol/L)	39.9	12.5	7.5	7.5	34.9 to 104.8 nmol/L
(ng/mL)	16.0	5.0	3.0	3.0	14.0 to 42.0 ng/mL
1,25 (OH) <sub>2</sub> vitamin D					
(pg/mL)	115.0	190.0	78.0	100.0	25.0 to 45.0 pg/mL
Hemoglobin					
(g/L)	131.0	86.0	130.0	94.0	100.0 to 120.0 g/L
(g/dL)	13.1	8.6	13.0	9.4	10.0 to 12.0 g/dL
Abnormal values are in bold.					

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N/A = not available.



FIGURE 1. Radiographs of a patient who has diffuse osteopenia, showing flaring and irregularity of the distal metaphyses of the long bones and fracture of the left femur.

2-year period. They demonstrate the variability of the clinical presentation of vitamin D deficiency rickets. Despite their different presentations (eg, convulsions, developmental delay, multiple fractures, and respiratory complaints), these patients have common historical findings, including being African-American and having diets deficient in vitamin D due to either unsupplemented breastfeeding or to reduced milk or dairy product intake. Although younger infants were primarily breastfed during the first year of life, older infants had low intakes of milk and dairy products. The associated low vitamin D intake was the key factor in the risk of developing vitamin D deficiency rickets. The normal serum creatinine and urea nitrogen levels made renal causes of rickets less likely. All of these patients exhibited the biochemical and skeletal features of vitamin D deficiency rickets.

Because they all lived in Michigan, the role of sunshine deprivation during the winter months is another significant factor in these cases.

These observations are consistent with research done by Specker and Tsang in the 1980s, who observed large seasonal differences in serum 25-hydroxyvitamin D concentration. Serum vitamin D levels were directly related to the amount of sunshine exposure.

### **Relevance to Primary Care**

Health maintenance is a fundamental component of the care of pediatric patients. It includes anticipatory guidance regarding growth, development, injury prevention, and nutrition. Diet history, especially a history of breastfeeding without vitamin D supplementation or low milk intake, should alert the clinician to the possibility of rickets.

Clinical assessment begins with asking appropriate questions when taking a nutritional history. Dietary intake of vitamin D for infants can be assessed by asking about type of feeding (breastfeeding or formula). Infants who consume 32 oz (approximately 1 L) of formula daily will receive 400 IU of vitamin D, which

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fulfills the daily allowance recommended by the United States Department of Agriculture. Older infants and toddlers who consume less than 400 IU of vitamin D daily are at increased risk for vitamin D deficiency rickets. Macrobiotic and vegan diets are low in dietary calcium and vitamin D.

Although pediatricians usually discuss nutritional information and give recommendations about dietary supplements, the advice may not be understood or may be ignored. The American Academy of Pediatrics publication Pediatric Nutrition Handbook recommends vitamin D supplementation for breastfed infants. However, physicians may not address this issue adequately during health supervision visits. A recent survey of pediatricians in San Diego found that 29% of respondents did not recommend supplemental vitamin D for breastfed infants.

It is estimated that 26% of infants in the United States are breastfed at 6 months of age. The Healthy People 2000 initiative has established a goal of breastfeeding for 50% of infants at 6 months of age. If primary care physicians do not emphasize the need for vitamin D supplementation, more breastfeeding infants will be at increased risk for rickets.

Although one of the patients in these case studies was younger than 1 year of age, the other three presented at older ages. As the interval between health supervision visits increases in the first year of life, there is a greater chance that patients who are in the process of developing rickets will not be detected by physicians. They may not be diagnosed until the more striking clinical features become obvious.

#### Epidemiology

Historically, vitamin D deficiency rickets has been more prevalent in cities in northern latitudes. Recent case reports from Minneapolis, Minnesota, and Toronto, Ontario, remind us that rickets remains a significant nutritional concern. Rickets also may be a concern for families that ascribe to vegan diets. Vitamin D deficiency is more common among breastfed than formula-fed infants. In addition, infants of color are at increased risk because of decreased production of vitamin D in the skin. Infants and toddlers who have decreased vitamin D and calcium intake because of dietary preference also are at increased risk for rickets. This includes infants who are on macrobiotic and strict vegan diets, which exclude dairy products.

#### **Pathogenesis**

Vitamin D is a prohormone. There are two sources of vitamin D—cholecalciferol and ergocalciferol. Vitamin D is produced endogenously in the skin following exposure to ultraviolet radiation (cholecalciferol or vitamin  $D_3$ ) or obtained exogenously from the diet (ergocalciferol or vitamin  $D_2$ ).

After exposure to ultraviolet B radiation, 7-dehydrocholesterol in the skin is converted to precholecalciferol. Precholecalciferol in converted to cholecalciferol through thermal isomerization. Ergocalciferol often is used to fortify dairy products. It is produced by irradiation of ergosterol, a plant sterol.

Because ergocalciferol and cholecalciferol undergo similar metabolism, we will refer to both of them as vitamin D. Vitamin D is hydroxylated in the liver to 25-hydroxyvitamin D and subsequently in the kidney to 1,25dihydroxyvitamin D. This active metabolite increases absorption of calcium from the intestine and mobilizes calcium and phosphorus from bone.

Infant formulas are supplemented with vitamin D to provide 400 IU/L. Concentrations of vitamin D in human milk range from 12 to 60 IU/L. The vitamin D content of human milk correlates with maternal 25-hydroxyvitamin D concentration and intake. Specker et al demonstrated that African-American mothers had significantly lower concentrations of vitamin D compared with Caucasian mothers. Breastfed African-American infants who are not receiving vitamin D supplements are at increased risk of developing rickets.

During the spring and summer months, infants generally are exposed to sufficient sunlight to prevent vitamin D deficiency, but during the colder winter months they spend less time outdoors and often are bundled in several layers of protective clothing. Less vitamin D is produced in the skin, and infants become more dependent on dietary sources.

Specker et al suggested a theoretical time frame for the development of vitamin D deficiency rickets. As 25-hydroxyvitamin D levels decrease, parathyroid hormone (PTH) levels increase. PTH increases the activity of enzyme 25-hydroxyvitamin D 1-alphahydroxylase. 1,25-dihydroxyvitamin D increases mobilization of calcium from the bone matrix.

If vitamin D concentrations are inadequate, calcium absorption from the gut is inadequate, and calcium concentrations begin to decrease. This decrease in serum calcium precedes a decrease in serum phosphate concentrations. PTH concentrations increase to counteract the decline in serum calcium concentrations. As PTH restores serum calcium concentrations, it increases phosphaturia, and serum phosphate concentrations decline. At this point, clinical features such as rachitic bone changes become apparent on radiographs and on physical examination. In a few weeks to months, calcium salts are mobilized, and bone matrix breakdown begins. As serum calcium levels fall, there is increased activity of PTH, which promotes calcium loss from the bone.

Mobilization of calcium salts and bone matrix breakdown are associated with an increase in alkaline phosphatase. Continued inadequate vitamin D intake eventually is associated with declines in both serum calcium and phosphorus concentrations as mineral absorption becomes inadequate to support normal serum calcium despite elevated PTH concentrations. Rachitic bone changes are usually florid when this occurs.

Bone does not calcify normally in the absence of calcium and phosphorus. The result is a frayed zone of nonrigid tissue (also called the rachitic metaphysis). This zone is characterized by flaring of the ends of the bones and the "rachitic rosary." This entire process occurs within a few months.

#### **Clinical Manifestations**

In a recent study, 10 of 18 patients were diagnosed as having vitamin D deficiency rickets during the course of routine pediatric care. They had a common history of unsupplemented breastfeeding beyond 6 months of age. Physical findings included decreased linear growth and bowing of the legs, and radiographic findings included decreased mineralization of the bone matrix. Among the laboratory findings were low serum calcium and phosphorous levels and elevated serum alkaline phosphatase.

In advanced stages, vitamin D deficiency frequently is associated with short stature and poor weight gain, especially among infants approaching their first birthdays (Table 2). By plotting the child's height and weight on conventional growth curves, stature can be assessed easily.

In many cases, physical findings may not be obvious or appreciated by even the astute clinician during the early stages of vitamin D deficiency rickets. Skeletal findings are the most striking clinical manifestations in rickets. These may be evident within several months after the onset of vitamin D deficiency. They include craniotabes, enlargement of the costochondral junctions, scoliosis and kyphosis, enlargement at the wrists and ankles, coxa vara, and weak muscle tone. Other rachitic changes include frontal bossing and rachitic rosaries (knobs along the anterior costochondral ridge). Respiratory infections and pulmonary atelectasis that are related to severe chest deformities frequently are associated with rickets.

#### Diagnosis

#### LABORATORY FINDINGS

When vitamin D deficiency is suspected, a primary concern is to determine if the child is at risk for convulsions or tetany related to low calcium levels. Measurements of calcium, phosphorus, PTH, and alkaline phosphatase concentrations can be used to evaluate the risk for convulsions or tetany as well as to determine the duration of and adaptation to the rachitic state. In addition, renal function tests and hydroxyvitamin D and dihydroxyvitamin D levels should be obtained before treatment is initiated to rule out rickets due to renal disease or other causes (Table 3). Appropriate sequencing of diagnostic tests will prevent confusing diagnostic and therapeutic goals during the evaluation (Fig. 2).

In diagnosing rickets due to vitamin D deficiency, assays for 25-hydroxyvitamin D and 1,25dihydroxyvitamin D may be most sensitive and specific. Changes in these forms of vitamin D precede other biochemical and clinical features of vitamin D deficiency. Sev-

## TABLE 2. Primary Presenting Problems in Infants and<br/>Children Who Have Rickets (n = 63)

Incidental finding on radiograph or physical examination	19	
Nonspecific musculoskeletal complaints	16	
Failure to thrive/small for age	5	
Delayed development	6	
Seizures	5	
Sibling who had rickets	4	
Tetany	2	
Weakness	1	
Drowsiness	1	
Reproduced with permission from Cosgrove L, Dietrich A. Rickets in breast-fed infants.		

Reproduced with permission from Cosgrove L, Dietrich A. Rickets in breast-fed infants. J Fam Pract. 1985;21:205–209.

#### TABLE 3. Differential Diagnosis of Vitamin D Deficiency Rickets

#### Metabolic Bone Disease

- Vitamin D-resistant rickets
- Vitamin D-dependent rickets
- Congenital rickets
- Osteogenesis imperfecta

#### **Renal Disease**

- Renal osteodystrophy
- Renal tubular acidosis

#### General

- Child abuse
- Trauma
- Prematurity
- Hyperphosphatasia
- · Primary chondrodystrophy

eral conditions, including trauma and osteogenesis imperfecta, can cause elevations in alkaline phosphatase. In addition, several endocrine abnormalities, including hypoparathyroidism, can cause alterations in calcium and phosphorus concentrations.

#### **RADIOGRAPHIC DIAGNOSIS**

Conventional radiographs can provide radiologic evidence of rickets. Generalized osteopenia, fractures, and fraying of the metaphyses of the long bones are common findings (Table 4).

#### DIFFERENTIAL DIAGNOSIS

Vitamin D deficiency rickets can be distinguished from vitamin D-resistant (hypophosphatemic) rickets and vitamin D-dependent rickets by serum assays of 25hydroxyvitamin D and 1,25dihydroxyvitamin D (Table 5). A defect in the proximal tubular

#### TABLE 4. Radiographic Findings in Vitamin D Deficiency Rickets

- Widening of metaphysis
- Cup-shaped metaphysis
- Osteopenia
- Rib flaring
- Multiple fractures in various stages of healing

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FIGURE 2. Diagnostic algorithm for vitamin D deficiency rickets.

reabsorption of phosphate and a defect in the conversion of 25-hydroxyvitamin D to 1,25dihydroxyvitamin D cause vitamin D-resistant rickets. Vitamin D-dependent rickets is caused by decreased or deficient activity of the enzyme 25-hydroxyvitamin D 1-alpha-hydroxylase. Other types of metabolic bone disease that may resemble vitamin D deficiency rickets include primary chondrodystrophy, hyperphosphatasia, and osteogenesis imperfecta. Among the clinical features of primary chondrodystrophy are bowing of the legs, short stature, and a waddling gait. However, this occurs in the absence of abnormalities in serum calcium, phosphorus, alkaline phosphatase, or vitamin D. The hallmark of hyperphosphatasia is excessively elevated serum levels of the bone isozyme of alkaline phosphatase. Significant growth failure is caused by osteoid proliferation in the subperiosteal bone, which results

<b>TABLE 5. Distinguishing Features of Different Types of Rickets</b>						
TYPE OF RICKETS	CAUSE	25-OH VITAMIN D	1,25 (OH) <sub>2</sub> VITAMIN D	PARATHYROID HORMONE	CALCIUM	PHOSPHORUS
Vitamin D deficiency	Low endogenous vitamin D	Decreased	Normal or increased	Increased	Decreased	Decreased
Vitamin D- resistant	Defect in tubular reabsorption of phosphate	Normal	Normal or decreased	Normal or increased	Normal	Decreased
Vitamin D- dependent	Reduced activity of 25(OH) 1-alpha- hydroxylase	Normal	Decreased	Normal or increased	Normal or decreased	Decreased

Pediatrics in Review Vol. 21 No. 9 September 2000 Downloaded from http://pedsinreview.aappublications.org/ at Health Sciences Library State Univ Of New York on January 24, 2012 in separation of the periosteum from the bone cortex. Findings include bowing and thickening of the diaphysis and osteopenia. Osteogenesis imperfecta is caused by a defect in type II collagen, which results in the formation of brittle bones that are fractured easily. The most common form of osteogenesis imperfecta is associated with hearing loss and blue sclerae. The diagnosis can be confirmed by performing a fibroblast biopsy. Affected infants often present with multiple fractures, which are in various stages of healing.

Rickets commonly is associated with renal disease and is due to the associated hypophosphatemia and phosphaturia found in renal tubular acidosis disorders, renal calcium loss, or uremia. The ensuing hypocalcemia produces a secondary increase in PTH secretion that eventually may result in renal osteodystrophy. This leads to the alterations in skeletal growth and remodeling that occur in children who have chronic renal disease. These abnormalities in mineral and bone metabolism are the result of progressive loss of nephrons from glomerular insufficiency and uremia.

Preterm infants also may present with rachitic bone disease. Very low-birthweight (<1,500 g) and low-birthweight infants who receive total parenteral nutrition (TPN) are at increased risk because of their low intake of calcium and phosphorus. These infants require higher amounts of calcium in their TPN formulations than is standard.

Congenital rickets results when maternal intake of vitamin D and calcium is low. In many cases, mothers are on macrobiotic or strict vegan diets. Affected newborns have very low calcium levels and may present with seizures or tetany in early infancy. Congenital vitamin D deficiency occurs early in infancy, in contrast to vitamin D deficiency rickets related to low vitamin D intake, which occurs in older infants.

Child abuse must be considered whenever a physician treats a child who has multiple fractures. As illustrated in one of the case presentations, it is important to perform a skeletal survey in addition to serum assays for vitamin D, alkaline phosphatase, calcium, and phosphorus if the history suggests vitamin D deficiency.

#### **Treatment and Management**

When rickets is suspected, it is imperative to prevent complications, including convulsions related to hypocalcemia. Patients who have critically low calcium and phosphorus levels must have the hypocalcemia corrected with supplemental calcium.

Vitamin D supplementation may be initiated once laboratory and radiologic tests confirm the diagnosis of vitamin D deficiency rickets. Most experts recommend administration of oral vitamin D supplementation (800 to 1,000 IU/d) until serum alkaline phosphate levels and skeletal deformities return to normal. Calcium also should be supplemented at levels of 1,000 mg daily.

In addition to supplemental calcium and vitamin D, it is important to recommend diets rich in calcium, especially for children on vegan diets, which are low in calcium. The calcium content of various foods is described in Table 6.

#### Prevention

The primary role of the pediatrician in the management of rickets is prevention. Primary prevention includes informing the public about the benefits of breastfeeding and the need for dietary supplementation with vitamin D. This community-based intervention is accomplished through physician advocacy or public service announcements in brochures and handouts for public distribution.

Secondary prevention involves

FOOD	AMOUNT	CALCIUM (MG)
Dairy products		
Milk, liquid*	1 c	300
Milk, powdered*	1 c	60
Cheese, natural or processed*	1 oz	200
Cottage cheese*	1/4 c	60
Yogurt*	1 c	300
Ice cream*	1/2 c	110
Cream cheese*	1 tbsp	10
Meat and other protein sources		
Meat, poultry, fish*	3 oz	10 to 20
Canned fish with bones*	3 oz	250
Egg*	1 egg	30
Cooked dried beans	1/2 c	70
Nuts and seeds	2 tbsp	20 to 40
Peanut butter	2 tbsp	20
Bread, cereal, pasta		
Bread	1 slice	25
Biscuits	1 roll	25
Corn tortilla	1 tortilla	60
Cooked and dry cereals	1 serving	15
Noodles, macaroni	1/2 c	15
Vegetables and fruits		
Vegetables, average	1/2 c	20 to 40
Green, leafy vegetables, average	1/2 c	100
Fruits, average	1/2 c	20 to 40
Calcium-fortified orange juice	1/2 c	160
*Not included in vegan diets.		

**TABLE 6. Calcium Content of Foods** 

Adapted from Ellyn RD. Child of Mine: Feeding with Love and Good Sense. Palo Alto, Calif: Bull Publishing Co; 1986.

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targeting high-risk groups, including African-American breastfeeding infants, children who have low intakes of milk and dairy products, and infants who live in northern areas where colder winter weather precludes outdoor activities. Although serum assays of 25-hydroxyvitamin D are most sensitive and specific for vitamin D deficiency, alkaline phosphatase levels can be measured in conjunction with hemoglobin in these high-risk infants to detect vitamin D deficiency.

Tertiary prevention involves management of patients similar to those discussed in the case presentations. Dietary supplementation helps to speed the healing process. Infants and children in whom rickets has been diagnosed should be managed appropriately to avoid such complications as hypocalcemia, seizures, and growth delay. Prompt recognition and careful education of caregivers about dietary changes and supplements will speed the healing process.

#### Prognosis

Outcomes for children diagnosed with vitamin D deficiency rickets are good. Rickets is not a fatal disease, and early diagnosis will prevent sequelae such as motor developmental delay. Supplementation with sufficient amounts of vitamin D begins the healing process within a few days and progresses slowly over several months. In many cases, the bony deficiencies may persist for months to years during treatment. Severe bowing of the legs may resolve within several years without surgical intervention. In advanced cases, however, knock-knees, curvature of the upper extremities, chest deformities, rachitic pelvis, coxa vara, and short stature may be permanent.

#### Summary

Although often considered a disease of the past, vitamin D deficiency rickets remains a serious nutritional disorder. Infants from darkerskinned ethnic groups as well as infants who are breastfed without receiving vitamin D supplementation are at higher risk. Vitamin D deficiency rickets can be diagnosed and managed by primary care physicians. Increased awareness of the possibility of rickets can prevent complications such as seizures, growth delay, and fractures.

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#### **PIR QUIZ**

Quiz also available online at www.pedsinreview.org.

- 6. Of the following, the *most* frequent presenting clinical finding in infants and children who have rickets is:
  - A. Failure to thrive.
  - B. Incidental finding on physical examination.
  - C. Seizures.
  - D. Tetany.
  - E. Weakness.
- 7. A 15-month-old boy who has lower limb bowing and frontal bossing has been primarily breastfed. He is diagnosed as having vitamin D deficiency rickets. Which of the following laboratory values would be *most* characteristic of this disorder?
  - A. Elevated 1,25-dihydroxyvitamin D.
  - B. Elevated 25-hydroxyvitamin D.
  - C. Increased serum phosphate.
  - D. Low alkaline phosphatase.
  - E. Normal parathyroid hormone.
- 8. Of the following, which child is at the *highest* risk for developing vitamin D deficiency?
  - A. Breastfed 7-month-old not receiving vitamin D supplementation.
  - B. Formula-fed 12-month-old.
  - C. Infant who has cow milk allergy and is receiving soy formula.
  - D. School-age child who is a picky eater and is receiving multivitamins.
  - E. Toddler who is drinking 2% skim milk.
- 9. Which of the following radiographic findings is *most* characteristic of a child who has vitamin D deficiency rickets?
  - A. Advanced bone age.
  - B. Broadened zone of divisional calcification.
  - C. Fraying of the metaphysis.
  - D. Subperiosteal hemorrhage.
  - E. Thickening of the diaphysis.

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