EDITORIAL

Vitamin D and rickets: much has been accomplished, but there is room for improvement

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It is time to consider serum screening to assess vitamin D adequacy during pregnancy with a view to protecting the offspring from rickets, especially among population subgroups at high risk for vitamin D deficiency. Recent reports from both sides of the Atlantic provide evidence that symptomatic vitamin D deficiency continues to occur occasionally in infants and young children, manifesting as hypocalcemic seizures and, in some instances, heart failure in the early months of life, with rickets occurring somewhat later.[1–4] In North Carolina USA, 30 infants with nutritional rickets were treated at two participating hospitals between 1990 and 1999.[1] All were African American, had been breastfed, and were not supplemented with vitamin D. Those who had been weaned had a history of poor intake of fortified cow's milk or other dairy products. In addition to bone deformities, growth failure was a common feature. In Manchester, UK, six cases of 'florid' rickets were diagnosed during a two-year time period (1995–1997); all were breastfed for prolonged periods without vitamin D supplementation.[2] The parents of four were recent immigrants; parents of the other two were postgraduate students. Four of the mothers wore concealing clothing. At four London hospitals, a review of case records between 1996 and 2001 identified 65 cases of vitamin D deficiency, including rickets and/or symptomatic hypocalcemia; 39 of the children were Asian, 24 Afro-Caribbean, and 2 Eastern European.[3] More recently, an audit of four other London hospitals over a 30-month period between 2006 and 2008 identified 74 infants under the age of one year with symptomatic vitamin D deficiency.[4] Once again, nearly all of the infants (92%) belonged to ethnic groups with pigmented skin; 27% of the cases presented with hypocalcemic seizures; failure to thrive and cardiomyopathy were additional clinical features.

In the mid-1600s, most children in crowded living conditions in northern Europe developed a severe bone-deforming disease characterized by growth retardation, enlargement of long bone epiphyses, leg and spine deformities, knobby bumps at the costochondral junction (now known as 'rachitic rosary'), and weak muscles with poor tone. During the 1800s, this cluster of deformities, labeled rickets, was empirically understood to be both treatable and preventable via exposure to sunlight, but studies in Boston and Leiden in the latter part of the 19th century showed varying degrees of rachitic deformities in 80–90% of autopsied children. By the 1940s, vitamin D supplementation was recommended to prevent rickets, and the disorder largely disappeared. The ability of the body to produce vitamin D actually qualifies it as a hormone, even though supplementation from external sources is necessary in the absence of adequate exposure to UVB rays from sunlight. Above 35° latitude, these rays are filtered out before reaching the ground during winter months, meaning that vitamin D cannot be produced from this source for about six months of the year.

Discovery of the pathway by which vitamin D becomes activated and de-activated in maintaining adequate calcium absorption and bone integrity has led to numerous studies over the past 40 years, aimed at better understanding this metabolic process. Measurement in serum of 25 hydroxy vitamin D [25(OH)D], the inactive precursor of 1,25 dihydroxy vitamin D (the active form), has proven to be the most reliable indicator of vitamin D status and has been applied in many studies involving pregnant women. Even when maternal serum 25(OH)D concentrations are in the deficient range during pregnancy,[5–7] intestinal absorption of calcium continues to be enhanced, due to pregnancy-specific factors unrelated to vitamin D that serve to protect both mother and fetus (e.g. PTH-related protein, estradiol, human placental lactogen).[8,9] This compensatory mechanism does not, however, extend beyond pregnancy for either the mother or the infant. In studies where 25(OH)D concentrations have been measured in paired maternal and cord sera, it has been demonstrated that the newborn depends on the mother for *in utero* transfer of vitamin D. Newborn and maternal 25(OH)D concentrations correlate strongly, and low maternal 25(OH)D often results in the infant being biochemically deficient in vitamin D during the first weeks after delivery.[6,7,10,11] Given this insight, any strategy aimed at avoiding symptomatic vitamin D deficiency in offspring would logically include assuring adequacy of maternal vitamin D during pregnancy.[3] Attending to this aspect of maternal and child health has added significance for mothers who breastfeed.

Preventing symptomatic vitamin D deficiency in infants and young children requires a co-ordinated public health initiative. Appropriate supplementation should be recommended for all pregnant women. In both the UK and North America, current guidelines call for 10 μg per day (400 IU) for the mother during pregnancy and while breastfeeding.[12,13] This level of supplementation is well below the amount necessary to induce toxicity in adults (>10,000 IU/day for >5 months).[14,15] In addition, the American Academy of Pediatrics recommends that infants be supplemented with 400 IU/day of vitamin D, beginning in the first few days of life (tolerable upper intake – 1,000 IU).[16,17] As the primary health target of intervention is the avoidance of rickets, it appears reasonable to focus particular attention on breastfeeding mothers and their infants, especially for racial groups with pigmented skin and those who wear concealing clothing. It may also be reasonable to

conduct research to determine whether screening for vitamin D deficiency via serum measurement of 25(OH)D is worthwhile, especially in high-risk groups.

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