A plea for vitamin D$^{1,2}$

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A number of cross-sectional and longitudinal studies have shown that the age of menarche is decreasing across the world (reviewed in reference 1). In this issue of the Journal, Villamor et al (2) suggest that vitamin D deficiency may be one explanation.

As one example, during the 20-y study period of the Bogalusa Heart Study, the median menarcheal age decreased by $\sim$9.5 mo among African American girls (from age 12.9 to 12.1 y) compared with a decrease of 2 mo among white girls (from age 12.7 to 12.5 y) from 1974 to 1994 (3), which shows potential ethnic-genetic influences on this trend. A decreasing age of menarche is not just an abstract academic concept but a factor associated with adverse consequences on future health. Numerous conditions including breast cancer occur with increased prevalence in those who experience an early age of menarche in many studies; for example, menarche at the age of $<12$ y increases the risk by $\sim$50% compared with girls who reach menarche at age 16 y (reviewed in reference 4). In disease-discordant monozygotic twins, the twin with cancer recalled puberty as being earlier than did the other twin; and in disease-concordant twins, the twin with earlier menarche had the earlier diagnosis of breast cancer (5).

Genetic factors play a major role in determining the age of menarche; thus, there is a high concordance within ethnic groups as well as between age of menarche in mothers and daughters (6). The correlation between mother-daughters should theoretically be equal to sister-sister ages of menarche if only genetic factors are operative, but because sister-sister correlations are higher than mother-daughter correlations, environmental influences are thought to add to genetic factors (7). A portion of this negative secular trend in menarche appears to be clearly related to the increasing prevalence of obesity in childhood. The longitudinal National Heart, Lung, and Blood Institute Growth and Health Study followed 1266 white and 1313 African American girls from 9 or 10 y of age for $\geq$10 y and found a correlation between increased weight and BMI and decreased age of menarche (8).

Other factors are postulated to affect the age of menarche, including socioeconomic conditions, energy expenditure, and states of health. Environmental factors are suspected to account for the decreased age of menarche found in northern latitudes compared with southern latitudes, as noted by Villamor et al (2), who included vitamin D status as a focus of this discussion.

The information identified by Villamor et al (2) showed that vitamin D deficiency correlates with a decreased age of menarche in a lower- and middle-economic-class population of children in Bogota, Colombia. These quite interesting but admittedly preliminary data offer a possible biological explanation for earlier age of menarche in higher latitudes where vitamin D values decrease. The authors found that the relation between earlier menarche and lower concentrations of vitamin D holds true after controlling for BMI, an important consideration because obese individuals tend to have lower serum concentrations of vitamin D as well as earlier menarche. As the authors point out, an interventional study ensuring adequate vitamin D intake in girls while relating their vitamin D concentrations in serum to the age of onset of menarche would be a welcome addition to the literature on this phenomenon. In addition, a survey studying serum concentrations of vitamin D and age of menarche across latitudes in a prospective manner would further advance the field.

Vitamin D deficiency is a prevalent condition in children and adolescents in the United States; it is found in sunny climates such as Las Vegas and Sacramento (9) as well as in the more equatorial latitudes of Bogota. Indeed, rickets has made a comeback in the United States and elsewhere, particularly in breastfed infants who are not supplemented with vitamin D and especially in those with darker skin tones who were born of mothers who themselves were vitamin D deficient. With the present decreased vitamin D and calcium intake in children (related to a remarkable decrease in milk and other dairy product intake), we have reason to worry about a future increased prevalence of osteopenia and osteoporosis. But numerous adverse health conditions are postulated to relate to vitamin D deficiency in addition to rickets and decreased bone mass. Among those garnering recent interest is an increased prevalence of insulin resistance in vitamin D–deficient individuals, leading to greater risk of many manifestations of the metabolic syndrome (10).

Obesity is an insulin-resistant state, and obese individuals tend to have lower vitamin D concentrations. Thus, there may be no surprise that both obesity and vitamin D deficiency are reported to increase the likelihood of metabolic complications in polycystic ovarian syndrome, which is itself an insulin-resistant state even without the burden of obesity (11).

Thus, in addition to early menarche, there are further relations between vitamin D and reproductive status that are ripe for further study. With the established relation between obesity and decreased age of menarche, these considerations offer a possible solution to the problem of early menarche. And with the proportional decrease in milk and other dairy products consumed by children, the explained relation between vitamin D deficiency and early menarche becomes even more apparent.
creased age of menarche and with the knowledge that low vitamin D concentrations are common in childhood and adolescence, added to the results of Villamor et al’s study (2) which implicates vitamin D deficiency with decreased age of menarche, we have all the more incentive to ensure adequate intake of vitamin D (and calcium) in our young population.

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REFERENCES