HHS Public Access

Author manuscript

JAMA Pediatr. Author manuscript; available in PMC 2021 July 28.

Published in final edited form as:

JAMA Pediatr. 2018 February 01; 172(2): 196–197. doi:10.1001/jamapediatrics.2017.4654.

Adaptation of Bone to Mechanical Strain

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In Reply We appreciate the discussion by Sugiyama of potential mechanism(s) by which height gain contributes to bone acquisition as described in our study.[1] Sugiyama raises several important points that deserve additional discussion.

First, he posits that a relatively low degree of mineralization, caused by high bone remodeling during growth, supports rapid increases in whole-body and skeletal site-specific BMC. This occurs because in the setting of decreased bone stiffness, there is increased bone strain and thus enhancement of mechanical strain-related stimuli, eg, as produced by physical activity and increasing height. We agree that physical activity benefits the pediatric skeleton; it is positively associated with bone *z* scores[2] as well as bone mineral accretion across all puberty stages. However, additional factors contribute to bone modelling and remodeling. We showed that variation near genes that potentially contribute to mechanosensation may also modulate the response to physical activity. In addition, numerous endocrine pathways are necessary for bone mineral accrual, and during puberty, insulin-like growth factor 1 and gonadal steroids are required to promote normal bone accretion. Thus, the mechanical strain-related stimuli of height gain and physical activity are only a part of the complex cascade by which peak bone gain is achieved.

Sugiyama also conjectured that the degree of skeletal mineralization could be estimated using biomarkers of bone turnover. Formation and resorption marker concentrations are high during growth owing to bone modeling and linear growth and do not lend themselves to predicting bone accrual. For example, bone-specific alkaline phosphatase is independently associated with puberty stage, sex, baseline whole-body bone mineral content, and height velocity in addition to whole-body bone mineral accrual.[3] Again, we emphasize the exquisite complexity of bone accretion during growth.

Sugiyama also conjectures that differences in physical activity and/or the response to mechanical strain-related stimuli could underlie observed increases in lean mass and bone mineral content in African American children. In our previous report on physical activity and bone accretion,[4] there were no ancestry group differences in physical activity among male participants, although African American girls had higher levels of physical activity than non–African American girls in puberty stages 4 and 5, long after ancestry differences in bone mass are established.[4] Ancestry-specific differences in bone and body composition are

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Conflict of Interest Disclosures: None reported.

of unknown etiology, but differences in the timing and pace of sexual and skeletal maturation could underlie some of the observed differences.[5]

Finally, Sugiyama noted that lower skeletal mineralization during childhood and increased risk for trauma influence fracture risk. Indeed, we previously showed that male sex, skeletal age between 10 and 14 years, lower body fat percentage, and sports participation have all been associated with increased fracture risk.[6] Also, even independent of sports participation, children of European descent had higher rates of fracture.

In sum, our report described sex- and ancestry-specific patterns of bone accrual. The mechanisms underpinning these patterns go beyond mechanostimulation and include genetics, population ancestry, sexual maturation, endocrine regulation, physical activity, and nutrition. The role of these factors in attainment of peak bone mass deserves additional study.

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