

Osteoporosis: Who is Guilty?

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The modern human skeleton represents an end point of million years of ongoing adaptation. The skeleton integrates several vital non-mechanical functions (mineral homeostasis, hematopoiesis) in conjunction with its primary purpose – locomotion – into a single organ.

Sex steroids, especially estrogen, play an important role in skeletal homeostasis¹. Estrogen is considered a bone conserving hormone² and its principal skeletal effect at the tissue level is suppression of bone turnover and maintenance of balanced rates of bone formation and bone resorption. Consequently, the loss of estrogen function at menopause is associated with a marked increase in the rate of bone remodeling and a negative balance between bone formation and bone resorption at the level of the bone multicellular unit (BMU) leading to bone loss. While the extraskelatal effects of estrogen (e.g., hypertrophy of the reproductive organs at puberty and atrophy at menopause) are considered perfectly normal for most reproductive tissues, somewhat paradoxically, this “ON at puberty – OFF at menopause” is not considered the same way for the skeleton. The prevailing pathomechanistic views consider the female skeletal mass that exists before menopause “normal”, and accordingly, the loss of mineral occurring at menopause “pathological”.

When Fuller Albright first described the disease called postmenopausal osteoporosis in 1940, he proposed the existence of estrogen-induced deposition of “reproductive bone” (medullary bone)³. Although this finding of the pubertal effects of estrogen on female bones was paramount to Albright when he devised his theory, it was not until 1998, that the existence of this phenomenon was truly “discovered” in humans⁴. By reanalyzing the data of whole body bone mineral content (TBMC) and body composition in Argentine boys and girls from 2 to 20 years of age⁵, Schiessl⁴ was able to show that the increase in bone mass in both sexes seems to closely follow the increase in lean body (muscle) mass until just prior to menarche, i.e., the onset of cyclic estrogen secretion. Thereafter, this uniform pattern in the development of male and female skeletons suddenly dissociated, as the female skeletal mass starts to increase rapidly and disproportionately to the concurrent increase in lean body mass⁴. This suggested that relative to the mechanical demands placed on bones, girls have substantially higher BMD than boys at the corresponding age. Gender studies

carried out in female rats showed that the ‘extra’ bone laid down at menarche was deposited in the trabecular compartment, while male rats optimized their bone structure mostly in cortical bone improving its geometry.

If estrogen indeed is responsible for deposition of extra stock of trabecular bone into the female skeleton at puberty, then shouldn't withdrawal of estrogen secretion at menopause result in unpacking of roughly the same amount of mineral? The data from a study by Ferretti⁶, in which TBMC and lean body mass were measured in a population of both genders between 2-87 years of age showed indeed, that at puberty the BMC/lean body mass-ratio in females reaches a higher level than that of males, and remains higher throughout the entire fertile period. At menopause, the BMC/lean body mass-ratio in females begins to decline rapidly and eventually exhibits comparable values to males, thus providing a quite convincing corroborative clinical evidence for the above noted packing and subsequent unpacking of bone at puberty and at menopause, respectively⁶.

So, what does this all mean? In females, the onset of estrogen secretion at puberty results in the deposition of a surplus of trabecular bone in the axial skeleton, an apparent evolutionary safety measure against the anticipated transient bone loss caused by late pregnancy and lactation. When the female reproductive capacity ceases at menopause, this bone stock is shed as redundant, serving as the origin of the type I postmenopausal osteoporosis^{7,8}. The female skeleton has to serve a dual purpose to serve its mechanical and reproductive functions. In the post-reproductive phase in the female, cortical geometry can no longer adapt sufficiently to substitute for the loss in mechanical stability caused by the shedding of the ‘reproductive’ cancellous bone compartment in the axial skeleton.

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