

BONE LOSS IN ADULTS EXPOSED A WEAK TERATOGENIC STRESS

Eugene Kobylansky

Tel Aviv University, Gray Faculty of Medical and Health Sciences, Department of Anatomy and Anthropology, Tel Aviv, Israel

Background: We hypothesized that some developmental toxicants (teratogens) given at a sub-threshold teratogenic dose can detrimentally affect bone health in adults. We also examined whether such teratogenic exposure depends on the embryonic genome.

Materials and methods: ICR mice as well as 57Bl/6J (C57) and C3H/HeJ (C3H) mice exhibiting a low (C57) and high (C3H) bone mass phenotype were exposed to a single injection of 5-aza-2-deoxycytidine (5-AZA) at a sub-threshold teratogenic dose (0.15mg/kg) on day 10 of gestation. Offspring were obtained and their femur was evaluated by micro-computed tomography (micro-CT). The activity of caspase 3 and miRNA expression (~380 miRNAs) were tested in embryonic hind limb buds collected 24 and 48 h after 5-AZA injection. Primary cultures of femoral stromal/osteoblastic cells and osteoclast precursor cells were used to test the expression of RANKL and OPG as well as the level of osteoclast formation by TRAP staining.

Results: Micro-CT revealed that femora of ICR 5-month-old male offspring exposed to 5-AZA had trabecular microarchitecture indicative of bone loss. In hind limb buds of embryos altered expression of some microRNAs demonstrated as regulators of key osteoblastogenic genes has been observed. Furthermore, the increased expression of RANKL in femoral stromal/osteoblastic cells of offspring of 5-AZA-treated females has been found. Finally, loss of bone quality was registered in C3H offspring but not in their C57 counterparts.

Conclusions: This study implies that: 1) low-dose exposure to a teratogen can induce bone loss in adult offspring and 2) offspring inherently exhibiting a low bone mass phenotype may be more resistance to an antenatal stress-induced bone loss than those inherently exhibiting a high bone mass phenotype.

Keywords: Low-dose teratogen exposure; Bone loss; Stress.