Progesterone as a bone-trophic hormone.

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Experimental, epidemiological, and clinical data indicate that progesterone is active in bone metabolism. Progesterone appears to act directly on bone by engaging an osteoblast receptor or indirectly through competition for a glucocorticoid osteoblast receptor. Progesterone seems to promote bone formation and/or increase bone turnover. It is possible, through estrogen-stimulated increased progesterone binding to the osteoblast receptor, that progesterone plays a role in the coupling of bone resorption with bone formation. A model of the interdependent actions of progesterone and estrogen on appropriately "ready" cells in each bone multicellular unit can be tied into the integrated secretions of these hormones within the ovulatory cycle. Figure 5 is an illustration of this concept. It shows the phases of the bone remodeling cycle in parallel with temporal changes in gonadal steroids across a stylized ovulatory cycle. Increasing estrogen production before ovulation may reverse the resorption occurring in a "sensitive" bone multicellular unit while gonadal steroid levels are low at the time of menstrual flow. The bone remodeling unit would then be ready to begin a phase of formation as progesterone levels peaked in the midluteal phase. From this perspective, the normal ovulatory cycle looks like a natural bone-activating, coherence cycle. Critical analysis of the reviewed data indicate that progesterone meets the necessary criteria to play a causal role in mineral metabolism. This review provides the preliminary basis for further molecular, genetic, experimental, and clinical investigation of the role(s) of progesterone in bone remodeling. Much further data are needed about the interrelationships between gonadal steroids and the "life cycle" of bone. Feldman et al., however, may have been prophetic when he commented; "If this anti-glucocorticoid effect of progesterone also holds true in bone, then postmenopausal osteoporosis may be, in part, a progesterone deficiency disease."