THE PATHOGENESIS OF
POST-MENOPAUSAL OSTEOPAenia
USING THE OOPHORECTOMISED RAT MODEL

Natalie Ann Sims B.Sc.(Hons)
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ABSTRACT

After the menopause in the human female, bone turnover is increased and bone density is reduced leading to increased fracture risk. The mechanisms by which oestrogen deficiency causes this bone loss remains unclear.

The mature oophorectomised rat is a well-recognised model of post-menopausal bone loss, and has been used in this thesis to study the effects of oestradiol on bone cells in vivo.

The immediate effects of oophorectomy (oestrogen-deficiency) were determined by the measurement of biochemical and histomorphometric markers of bone formation, resorption and trabecular bone morphology from time of operation until 21 days post-operation. From this study a model of oestrogen-deficiency bone loss is proposed whereby the immediate increase in bone resorption results in increased activation frequency of bone turnover units, thus increasing the risk of trabecular perforation. Increased bone formation is delayed in oestrogen deficiency, such that the balance of bone turnover is maintained at the cellular level, however due to trabecular perforation, not all resorbed pits continue through to the formation stage, since bone formation requires a surface to build on.

A study of similar design was carried out to determine the effects of oestradiol on bone loss in oophorectomised rats. Oestrogen treatment of oophorectomised rats from the time of operation delayed trabecular bone loss by inhibiting both formation and resorption. Data from this thesis support a model of a direct inhibitory oestrogen action on both osteoclasts and proliferating osteoblasts as reported in vitro. These direct inhibitory effects of oestradiol appear to suppress the direct stimulatory action of oestrogen on mature osteoblast reported in vitro, and immediately following oestradiol treatment in this study.

The effects of salmon calcitonin and PTH-Pt(107-139) were also assessed in vivo using similar methods. The effects of these hormones on bone cell activity and trabecular bone loss in oophorectomised rats has been compared to the effects of oestradiol.
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