

# OSTEOSCOOP

News on current events in osteoporosis and rheumatology

## Glucocorticoid-induced osteoporosis: a defect in bone formation

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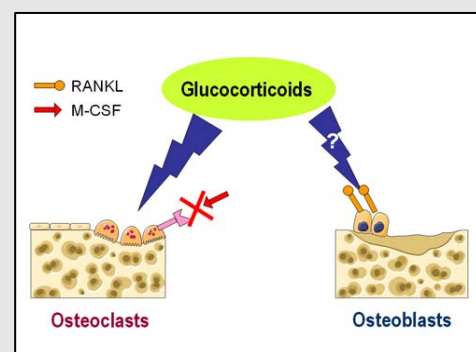
Glucocorticoids (GCs) are central to the treatment of inflammatory and immune disorders. These steroids, however, profoundly impact the skeleton, particularly when administered at high doses for prolonged periods, causing one of the most crippling forms of osteoporosis. Although the effect of GCs on osteoblasts is well documented (decreased number related to apoptosis), the mechanism underlying their effect is less clear because they do not seem to act directly on bone-forming cells. A recent study [1] affords new insight into the mechanism of action of GCs. Although that GCs slow down osteoblast differentiation, they stimulate RANKL synthesis, but, paradoxically, do not increase bone resorption. Instead, reduced bone remodeling is observed, related to a direct effect of GCs on osteoclasts. The half-life of these bone-resorbing cells is increased because of reduced cell death by apoptosis, while their ability to resorb bone is impaired, due to cytoskeleton abnormalities preventing osteoclasts from anchoring efficiently bone and developing an adequate brush border. The response of osteoclasts to M-CSF, a cytokine produced by osteoblasts, is specifically impaired. Invalidation of the GC receptor in osteoclasts by genetic engineering restores a normal phenotype of osteoclasts, and results in recovery of normal bone formation.

This study provides evidence that impaired resorption may lead to impaired bone formation. It remains to be established whether lazy osteoclasts remain too long on bone surfaces or a more complex signal prompts osteoblasts to reduce their activity.

1. Kim H-J. et al. *J Clin Invest.* 2006;116:2152-2160.

### Glucocorticoids (GCs) affect osteoblasts and osteoclasts

GCs decrease the number of osteoblasts because they induce apoptosis of these cells. Meanwhile, they increase the expression of RANKL. However, GCs slow down bone turnover because activation of osteoclasts is impaired as a consequence of the lack of response of these bone-resorbing cells to M-CSF. The overall effect of GCs is therefore to prevent osteoblasts colonizing resorbed bone surfaces and forming new bone.



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