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News on current events in osteoporosis and rheumatology

Impaired gastric acidification negatively affects calcium homeostasis and bone mass

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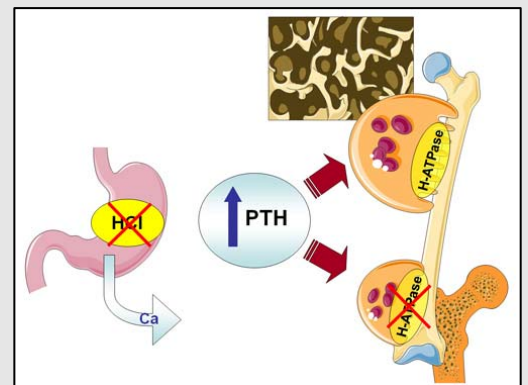
Activation of osteoclasts and their acidification-dependent resorption of bone is thought to maintain proper serum calcium levels. In a recent study [1], the authors show that osteoclast dysfunction alone does not generally affect calcium homeostasis. Indeed, mice deficient in Src, encoding a tyrosine kinase critical for osteoclast activity, show signs of osteopetrosis, but without hypocalcemia or defects in bone mineralization. Mice deficient in a gastrin receptor that affects acid secretion by parietal cells have the expected defects in gastric acidification but also secondary hyperparathyroidism and osteoporosis and modest hypocalcemia. These results suggest that alterations in calcium homeostasis can be driven by defects in gastric acidification, especially given that calcium gluconate supplementation fully rescues the phenotype of the gastrin receptor-mutant mice. Finally, mice deficient in a subunit of the vacuolar proton pump specifically expressed in osteoclasts and parietal cells show hypocalcemia and osteopetrorickets. Although neither Src- nor gastrin receptor-deficient mice have this latter phenotype, the combined deficiency of both genes results in osteopetrorickets.

In conclusion, the authors find that osteopetrosis and osteopetrorickets are distinct phenotypes, depending on the site or sites of defective acidification.

1. Schinke T et al. *Nat Med.* 2009;15: 674-681.

Impaired gastric acidification negatively affects calcium homeostasis and bone mass

Normal gastric acid secretion is mandatory for appropriate calcium absorption. In case of deficient gastric secretion, calcium absorption is decreased and hypersecretion of PTH occurs. The consequences on bone of this disorder depend on the activity of osteoclasts. In case of normal osteoclast function, bone resorption is increased and osteoporosis develops. However, in case of deficient osteoclasts with impaired proton ATPase activity, PTH-induced bone resorption is blocked, resulting in severe hypocalcemia and osteopetro-rickets.



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