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Acidosis, hypoxia and bone.

Arnett TR.

Bone homeostasis is profoundly affected by local pH and oxygen tension. It has long been recognised that the skeleton contains a large reserve of alkaline mineral (hydroxyapatite), which is ultimately available to neutralise metabolic H(+) if acid-base balance is not maintained within narrow limits. Bone cells are extremely sensitive to the direct effects of pH: acidosis inhibits mineral deposition by osteoblasts but it activates osteoclasts to resorb bone and other mineralised tissues. These reciprocal responses act to maximise the availability of OH(-) ions from hydroxyapatite in solution, where they can buffer excess H(+). The mechanisms by which bone cells sense small pH changes are likely to be complex, involving ion channels and receptors in the cell membrane, as well as direct intracellular effects. The importance of oxygen tension in the skeleton has also long been known. Recent work shows that hypoxia blocks the growth and differentiation of osteoblasts (and thus bone formation), whilst strongly stimulating osteoclast formation (and thus bone resorption). Surprisingly, the resorptive function of osteoclasts is unimpaired in hypoxia. In vivo, tissue hypoxia is usually accompanied by acidosis due to reduced vascular perfusion and increased glycolytic metabolism. Thus, disruption of the blood supply can engender a multiple negative impact on bone via the direct actions of reduced pO(2) and pH on bone cells. These observations may contribute to our understanding of the bone disturbances that occur in numerous settings, including ageing, inflammation, fractures, tumours, anaemias, kidney disease, diabetes, respiratory disease and smoking.