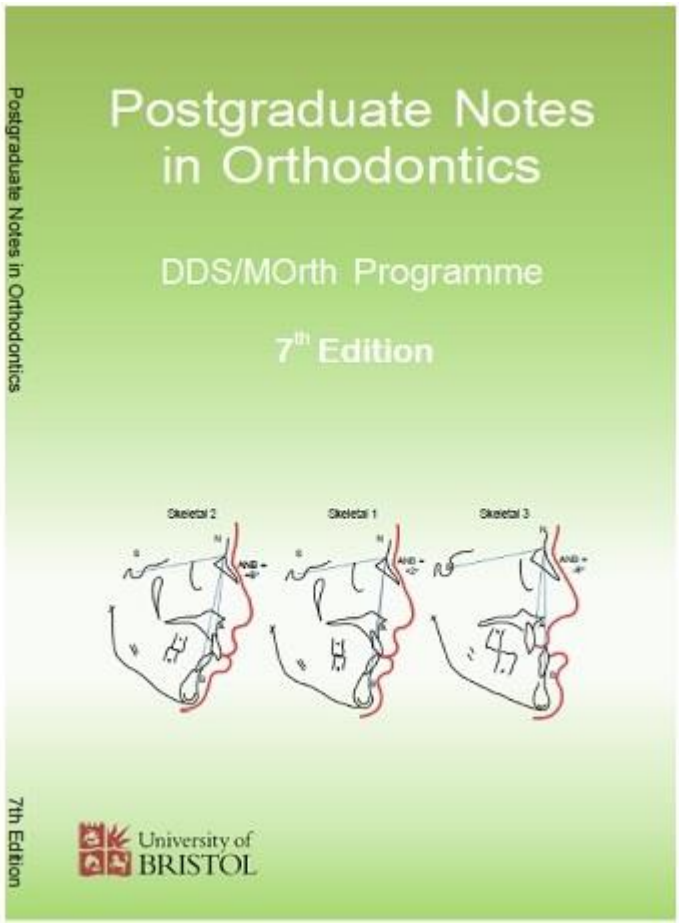

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Question and Answer Section 289

Example of layout of beginning of chapter, all chapters are fully referanced:

Bone Metabolism

Definition

Bone turnover refers to the total volume of bone that is both resorbed and formed over a period of time, usually expressed as percent/year; can be estimated by measuring relevant bone biomarkers — **Parfitt, 2002**

Bone remodelling - an active process of resorption and formation throughout skeleton, essential for calcium homeostasis and preserving the integrity of skeleton, through coupled activity of osteoclasts and osteoblasts; in adults, bone turnover occurs mainly through bone remodelling

Bone

Consists of

- inorganic mineral component i.e. calcium hydroxyapatite (2/3 of its weight)
- osteoid or organic matrix (1/3 by weight) mostly Type 1 collagen (90%) and small amounts of non collagenous proteins such as growth factors, osteonectin, osteocalcin and proteoglycans
- cells

Cells involved

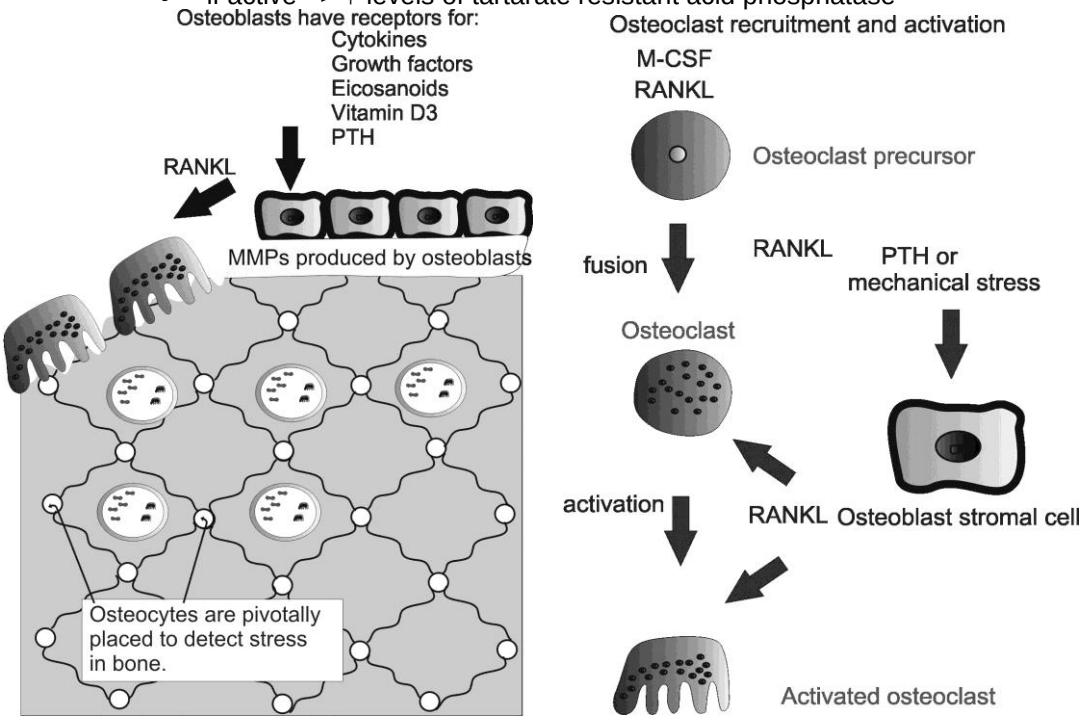
Osteoblasts

- are bone forming cells which line bone
- arise from undifferentiated mesenchymal cells e.g. from periodontal ligament
- mesenchymal cells differentiate through the immature pre-osteoblast state to the mature, functional osteoblast state
- synthesises both collagenous and noncollagenous bone proteins when mature, which constitute the organic matrix or osteoid
- defects in osteoid synthesis e.g. Type I collagen, can lead to serious disorders such as osteogenesis imperfecta
- produce RANKL and are responsible for osteoclast recruitment and activation — **Meikle, 2002, 2006**
- produce Osteoprotogerin (OPG) decoy receptor for RANKL which inhibits the differentiation of osteoclasts, suppresses their activation and induces osteoclast apoptosis (cell death). These are important controls of bone remodelling
- to protect bone and so also ↓ the amount of tooth movement
- have receptors for most of the bone resorbing hormones such as parathyroid hormone, cytokines such as RANKL, prostaglandins, 1,25-Dihydroxy-vitamin D3
- defects in osteoblast differentiation and maturation can lead to wide-ranging lethal disorders
- if active, => ↑ levels of alkaline phosphatase

Osteoclast

- is the main bone resorption cell
- arise from monocytes e.g. from blood
- multi-nucleate cell with ruffled border and receptors for few hormones, e.g. calcitonin and retinoic acid
- under direct and indirect control from hormones and growth factors
- osteoclasts cannot resorb bone without prior activation by the osteoblast
- a principle activator of osteoclasts is RANK Ligand (RANKL), a cell surface protein expressed on osteoblasts
- osteoclasts have receptors for RANKL

- RANKL is also important for the differentiation of osteoclasts from monocytic precursors
- if active => ↑ levels of tartarate resistant acid phosphatase



Bone resorption sequence

A hormone e.g. prostaglandin E_2 (PGE_2) binds to a receptor on the osteoblast → signal transduction plus osteoblast response
Osteoblast response:

1. produces soluble mediator for activation and recruitment of osteoclast (RANKL)
2. produces matrix metallo proteinases (MMP's) for breakdown of non mineralised osteoid layer
3. once osteoid is removed mineralised matrix is exposed and osteoclasts can remove bone

Krishnan & Davidovitch, 2006

Bone Formation

- osteocytes (osteoblasts incorporated into mineralised bone matrix) are situated in a rigid matrix and are thus ideally positioned to detect changes in mechanical stresses
- they could signal to surface lining osteoblasts and thus bone formation and indeed bone resorption may result
- control of osteoclast cell death important in overall control of bone remodelling

Bone Matrix

- bone is an enormous reservoir for many growth factors such as:
  i. *platelet derived growth factor* (PDGF)
  ii. *insulin like growth factors I and II* (IGFI and IGFII)
  iii. *bone morphogenetic proteins* (BMP) - these are part of the transforming growth factor beta (TGFβ) superfamily and are important inducers of bone formation
- some of these growth factors, e.g. fibroblast growth factor (FGF) are bound to heparin sulphate within bone
- others such as TGFβ or IGFII have distinct binding proteins to keep the growth factors in the bone matrix
- most of these growth factors are in a latent (non-active) form → acid conditions created by the osteoclasts for mineral dissolution may:
  a) cleave growth factors from their binding proteins and
  b) release them from latency

Krishnan & Davidovitch, 2006