Aims and objectives

To define and identify the function and roles of each of the following:

• Bone structure
• Cells in Bone
• Intramembranous vs endochondral
• Bone remodelling and mechanical forces
• Biology of Fracture Repair
Why do we have bones?

1. Support and protection
2. Movement
3. Store for metabolic calcium
4. Store for bone marrow
<table>
<thead>
<tr>
<th></th>
<th><strong>BONE</strong></th>
<th><strong>CARTILAGE</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Consistency</strong></td>
<td>mineralised hard tissue</td>
<td>permeable hydrated gel</td>
</tr>
<tr>
<td><strong>Organic matrix</strong></td>
<td>90% collagen (Type I)</td>
<td>40% collagen (type II + minor colls)</td>
</tr>
<tr>
<td></td>
<td>4% proteoglycans</td>
<td>60% proteoglycans</td>
</tr>
<tr>
<td><strong>Growth</strong></td>
<td>appositional</td>
<td>interstitial</td>
</tr>
<tr>
<td><strong>Nutrition</strong></td>
<td>dependent on blood supply</td>
<td>avascular</td>
</tr>
</tbody>
</table>
Bone matrix = gold mine of growth factors

BMPs - stimulate cells to become skeletal cells

TGFβs – chondrogenesis / osteogenesis

IGFs - cell proliferation

FGFs - angiogenesis

PDGF - chemotaxis
Bone types - terminology

**Based on developmental origin:**

endochondral vs intramembraneous

**Based on location:**

Cortical vs medullary bone
Bone types - terminology

Based on gross structure:

dense, compact bone vs
cancellous = trabecular = spongy

Based on microscopic structure:

fine lamellar bone (=cortical = compact)
vs woven bone (immature)
Compact bone: Haversian systems
Compact bone: Osteons
Trabecular bone
The cells of bone: osteoblasts

- Located on active bone-forming surfaces
- Produce osteoid
- Initiate mineralisation
- Become bone lining cells or osteocytes
The cells of bone: osteocytes

- Located within all living bones
- Connected via canaliculi
- Mechanoreceptors
The cells of bone: osteoclasts

- giant multinuclear cells
- are attracted to and resorb mineralized bone
- solubilise the mineral at low pH
- phagocytose the organic matrix
- require factors from osteoblasts
Bone development

Bone matrix must always be deposited on top of “something”

1. Membrane
   Intramembranous bone formation

2. Cartilage
   Endochondral bone formation

3. Pre-existing bone
Intramembraneous bone formation

Skull of 11-week foetus:
Foci of intramembraneous bone

Foci fuse to form network and, later, plate

19-week old foetus:
TS through calvarium
Endochondral bone formation

~ 8 weeks

~ 10 weeks

~ 8 months

~ birth
The growth plate
Indian hedgehog – PTH related protein feedback loop

Perichondrium

PTHrP

Ihh

PTHrP receptor

PTH/PTHrP receptor
Blomstrand chondrodysplasia

Mutations in PTH/PTHrP receptor
Mechano-transduction
Bone modelling during development
Remodelling unit

= BMU

Bone multicellular unit
Remodelling

- Adult skeleton remodelled every 10 years
- 3-4 million BMUs initiated each year
- 1 million BMUs operating at any one time
The remodelling process

1. Osteoclasts attracted to site
2. Osteoclasts resorb a packet of bone
3. Osteoblasts fill in defect
4. Osteoblasts attract to bone resorption pit
5. Osteoblasts become osteocytes

Osteoclasts

Osteoblasts
Bone re-modelling animation – normal bone

To view the animation of the normal bone re-modelling process double click on the box below.
Remodelling – why advantageous?

- enables adaptation to mechanical loading
- enables fracture healing
- prevents “bone fatigue” by continually renewing bone matrix
Lanyon’s turkey ulna experiments

TS through normal ulna

Not loaded for 8 weeks

High load for 8 weeks
Lanyon’s turkey ulna experiments

A) TS through ulna

B) 6 weeks Ca insufficiency

C) 6 weeks no Ca + no loading
Biology of Fracture repair
How to mend a fracture

1. Stop the blood flow
2. Inflammatory cells and macrophages
3. Release cytokines, “call” osteoblasts
4. Produce new bone matrix
5. Lay down layer after layer of new bone
6. Re-establish blood supply
How to mend a fracture

1. Stop the blood flow
Stage 1: Haematoma

Release of bioactive factors
- Inflammatory cytokines
- Growth factors

Release of growth factors from bone matrix
How to mend a fracture

2. Inflammatory cells and macrophages
Stage 2: Inflammation

Necessary for removal of debris

Increased by crushing injury and excessive motion

Decreased by anti-inflammatory drugs
How to mend a fracture

3. Release cytokines, “call” osteoblasts
Stage 3: Granulation tissue

- Intermediate tissue
- Contains collagen fibres
- First new blood vessels
Stage 4: Soft callus (cartilage)

Cartilage can expand quickly by interstitial growth.
Stage 4: Soft callus

- “call” mesenchymal stem cells
- stimulate their proliferation
- “push” these to differentiate to chondrocytes
- produce cartilage matrix – external callus
How to mend a fracture

4. Produce new bone matrix
Stage 5: Hard callus (endochondral bone)

- vascular invasion and resorption of cartilaginous callus
- migration of mesenchymal stem to non-resorbed cartilage struts
- proliferation of stem cells
- differentiation to osteoblasts
- bone matrix along cartilage struts
How to mend a fracture

5. Lay down layer after layer of new bone
Fracture callus – 4 weeks (rabbit)

- periosteum
- cartilaginous callus
- hard callus
- hard callus
- original bone shaft
- intramembraneous bone formation
- Fracture site
We’ve covered:

• Bone structure
• Cells in Bone
• Intramembraneous vs endochondral
• Bone remodelling and mechanical forces
• Biology of Fracture Repair
GLOBAL ORGANIZATION

Blood vessel + nerve

Osteon

Periosteum

Trabecular bone

Cortical Bone