Osteoporosis and the Aging Skeleleton

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Lecture Outline

- Basic definitions
- Changes in calcium metabolism with aging
- Hormone regulation of bone metabolism
- Epidemiology of osteoporosis & fractures
- Osteoporosis in men
- What a DXA bone density scan tell us – a real world example
- Treatment
Definitions
Definitions

- **Osteoporosis**, or porous bone, is a disease characterized by low bone mass and structural deterioration of bone tissue, leading to bone fragility and an increased susceptibility to fractures.

  National Osteoporosis Foundation
  (www.nof.org)
Definitions

• **Bone Mineral Density (BMD):** a measure of the mineral content of bone per volume, usually estimated through a DXA scan and expressed as grams per cubic centimeter (g/cc). Also referred to as bone mass.
Definitions

• Composition of bone:
  – 35% organic components (cells, fibers, collagen, etc.)
  – 65% inorganic mineral salts (mostly calcium phosphate)
Definitions

- **Osteoblasts**: form new bone (build)
- **Osteoclasts**: resorption of old bone (chew)
- **Osteocytes**: mature bone cells that maintain the bone matrix

Osteogenesis is the formation of new bone
Definitions

- **Periosteum** is a membrane of connective tissue that covers the outer surface of the bone
- **Endosteum** a thinner membrane covering the inner bone surfaces (that is, the trabeculae)
- Both contain both osteoclasts and osteoblasts
Definitions

• Types of bone:
  – compact bone (also known as cortical bone)
  – spongy bone (also known as trabecular or cancellous bone)
  • Small pieces of bone in the spongy part are called trabeculae
Figure 21-1
Definitions

• Bone remodeling is the formation and break down of bone
• Resorption is the break down of bone
• Bone is constantly remodeled
• Why is bone remodeled?
  – To maintain concentrations of $\text{Ca}^{2+}$ and $\text{PO}_4^{3-}$
  – To respond to mechanical stress
Bone Remodeling Sequence

- Oc Precursor
- Osteoclast
- Mononuclear Cells
- Ob Precursors
- Osteoblast

Resting Bone Surface

- Resorption
- "Activation"
- Reversal
- Bone Formation
- Mineralization

LC = Lining Cells  CL = Cement Line  OS = Osteoid  BRU = Bone Remodeling Unit

~3 WEEKS ~3 MONTHS

Osteoporosis and the Aging Skeleton
Definitions

- Micro-architecture of bone
- A trabeculae

Osteoporosis and the Aging Skeleton
Calcium Metabolism
Calcium Metabolism

- Extracellular calcium levels are highly regulated
- Need for calcium increases with age
  - Young adults: 800 mg
  - Women over age 50: 1500 mg
- Increased calcium needs may be explained by worsening absorption of dietary calcium
Calcium Metabolism

- **Parathyroid hormone**
  - Increases bone resorption, thus elevating plasma calcium

- **Calcitonin**
  - Lowers circulating calcium by inhibiting bone resorption

- **Calcitriol (Vitamin D3)**
  - Increases calcium absorption in intestine, decreases renal excretion and enhances bone resorption
Hormone Regulation of Bone Metabolism

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Hormone Regulation of Bone Metabolism

- Estrogen
  - Is likely to be protective against resorptive effects of parathyroid hormone
  - Obese women have greater bone mass
    - Might be due in part to higher levels of circulating estrogen
    - Heavier women have greater mechanical stress on their bones
Hormone Regulation of Bone Metabolism

• Glucocorticoids
  – Lower plasma calcium levels, which in turn may cause increased bone resorption, leading to osteoporosis

• Growth hormone
  – Net increase in calcium absorption and stimulates protein synthesis in bone
Hormone Regulation of Bone Metabolism

- Thyroid hormones
  - Induce hypercalcemia and hypercalciuria and may induce osteoporosis

- Insulin
  - Promotes bone formation (but there is bone loss among diabetics)
Epidemiology of Fractures & Osteoporosis
Epidemiology of Fractures & Osteoporosis

Skeletal fragility

Falls

Fractures

Osteoporosis and the Aging Skeleton
Epidemiology of Fractures & Osteoporosis

- One in two women and one in four men over the age of 50 will have an osteoporosis-related fracture
- 1 to 1.5 million osteoporotic fractures occur annually, including 300,000 hip fractures
- Osteoporotic fractures cost $17 billion dollars in 2001
## Epidemiology of Fractures & Osteoporosis

<table>
<thead>
<tr>
<th>Condition</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osteoporotic fractures</td>
<td>1,000,000+</td>
</tr>
<tr>
<td>Heart attack</td>
<td>513,000</td>
</tr>
<tr>
<td>Stroke</td>
<td>228,000</td>
</tr>
<tr>
<td>Breast cancer</td>
<td>182,000</td>
</tr>
<tr>
<td>Uterine cancer</td>
<td>32,800</td>
</tr>
<tr>
<td>Ovarian cancer</td>
<td>26,600</td>
</tr>
<tr>
<td>Cervical cancer</td>
<td>15,800</td>
</tr>
</tbody>
</table>

Epidemiology of Fractures & Osteoporosis

Cooper et al. JBMR 1992
Epidemiology of Fractures & Osteoporosis

- Who is at risk?
  - Smokers
  - Current low bone mass
  - Women
  - Small (thin, short) frame
  - Estrogen deficiency
  - Low lifetime Ca^{2+} intake
  - Vitamin D deficiency
  - An inactive lifestyle
  - Excessive use of alcohol
  - Being Caucasian or Asian
  - Involuntary weight loss
Epidemiology of Fractures & Osteoporosis

• Genetics
  – Family history of fracture increases risk by about 2X
  – Over 60% of bone mass is inherited
  – Search for common genes: unsuccessful so far.
Epidemiology of Fractures & Osteoporosis

• ALL types of fractures increase with decreasing BMD
  – *Except* fractures of face and fingers.

• Fractures due to severe trauma are “osteoporotic.”
  – are related to low BMD
  – Indicate an increased risk of future low trauma fractures
Epidemiology of Fractures & Osteoporosis

- Annual consequences of hip fractures
  - 24% will die from complications
  - 25% will require long-term care
Epidemiology of Fractures & Osteoporosis

• Vertebral fractures
  – Hunched over posture
  – loss of height
  – **NOT** normal aging
  – Most vertebral fractures occur between T6 and L3
Osteoporosis in Men
Osteoporosis in Men
Osteoporosis in Men

• Men have about \( \frac{1}{2} \) the risk of fracture
• Develop greater bone mass during growth.
  – Larger bones
  – Higher BMD
• No menopause with accelerated bone loss?

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Osteoporosis in Men

• Men have worse outcomes after hip fracture than women
  – One year mortality after hip fracture is twice as high for men as women
• 20% of those with osteoporosis are men
The DXA Scan
A DXA scan . . .

- **Dual Energy X-ray Absorptiometry**
A DXA scan ...

- A picture of the hip
- Estimates of volumetric BMD using a two dimensional picture
- Also done for the whole body and spine
A DXA scan

- BMD value is compared to a normal, or reference, population
- The normal population can be either age-matched or a young population
- Young population is generally ~30 year old (when bone mass is highest)
A DXA scan . . .

• T-score is used to diagnose disease
  – **Normal**: T-score higher than –1
  – **Osteopenia** (low bone mass): T-score between –1 and –2.5
  – **Osteoporosis**: T-score of –2.5 or less

• This is the World Health Organization criteria
A DXA scan . . .

• *Young* normal population gives a **T-score**

\[
\text{T-score} = \frac{\text{individual BMD level} - \text{young normal mean}}{\text{Standard deviation of young normal population}}
\]

• *Age-matched* normal population gives a **Z-score**

\[
\text{Z-score} = \frac{\text{individual BMD level} - \text{age matched mean}}{\text{Standard deviation of age matched population}}
\]
A DXA scan ...

- T-score
- Used for diagnosis of osteoporosis
- As with the picture, also done for the whole body and spine
Other methods to measure BMD

- Ultrasound
- QCT
- Emerging technologies ...
Treatment

• Bisphosphonates
  – Alendronate (Fosamax) and Residronate (Actonel)
  – Prevent bone breakdown; maintain or increase BMD; decrease risk of spine fracture and hip fracture
  – Side effects: stomach irritation

• Selective Estrogen Receptor Modulators (SERMs)
  – Raloxifene (Evista)
  – Maintains/increases BMD; decreases vertebral fracture risk; reduces breast cancer risk
  – Side effects: Leg cramps (occasionally), blood clots (unusual), worse hot flashes
Treatment

- **Estrogen**
  - Increases bone density; *may* reduce fracture risk; effects on many other organs
  - Side Effects: Many … heart disease, others

- **Calcitonin (Miacalcin)**
  - Prevents bone breakdown, helps maintains BMD; not clear how much it reduces fracture risk
  - Nasal irritation?
References

Physiological Basis of Aging and Geriatrics

Human Anatomy, Elaine N. Marieb and Jon Mallatt, editors