Osteoporosis
and the Aging Skeleton

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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

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

• Osteogensis 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
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 Ca$^{2+}$ and PO$_4^{3-}$
  – To respond to mechanical stress
Bone Remodeling Sequence

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

Resting Bone Surface → Resorption → CL → Reversal → Bone Formation → Mineralization

~3 WEEKS

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

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
CALCULUM INTAKE
800 mg/d YOUNG ADULTS
1500 mg/d WOMEN > 50 yr

OSTEODYNIC FACTORS

OSTEOLYTIC FACTORS

FREE CALCIUM

1,25-(OH)₂ D₃

CALCIUM LOSS = CALCIUM INTAKE

EXCRETION
KIDNEY

CALCIUM IN BLOOD AND TISSUE FLUIDS

1,25-(OH)₂ D₃

EXCRETION
KIDNEY

URINE

FECES

吸收
GI TRACT

钙

钙
Hormone Regulation of Bone Metabolism
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>Cases</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?
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**

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

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

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

- T-score
- Used for diagnosis of osteoporosis
- As with the picture, also done for the whole body and spine

Osteoporosis and the Aging Skeleton
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?

Osteoporosis and the Aging Skeleton
References

Physiological Basis of Aging and Geriatrics

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