Aging of the Skeleton: Osteoporosis

An Evolutionary and Biocultural Perspective
Aging and Skeleton

- **Aging and Senescence**: signs and the process of becoming old, less capable of homeostasis function (body cannot heal and is susceptible)
- Decline in many body functions: cardiac output, pulmonary and renal function, immune system
- Increase in chronic and degenerative diseases: osteoarthritis
- Bone loss: osteoporosis
Osteoporosis

• A reduction in bone mass and deterioration bone microstructure
• Clinically recognized as bone fragility with an increased susceptibility to fracture
• Osteopenia vs. osteoporosis
• Serious health concern in western aging populations: 1/2 women and 1/4 men > age of 50 will have an osteoporosis-related fracture. Women 4x times more
Osteoporosis

- Bone mineral density (BMD)
  - WHO definition: BDM 2.5 SD’s below young adult mean
- Measured with densitometry
- Problems: population specific, overlap in fracture and non-fracture BMD, only looks at one measure of bone (quantity)
Osteoporosis

- Factures hip, distal forearm, vertebral and hip fractures
- bone resorption > bone formation
Bone

- It is a rigid connective tissue
- **Organic** (1/3) and **Inorganic** (2/3)
Bone has

• structural function:
  - framework for soft tissue, muscles, protects vital organs

• physiological function:
  - reservoir marrow and hemapoetic tissue (rbc, white bc, platelets)
  - storage for adipose
  - stores Ca and Ph, linked to blood system
  - 90% of Ca and Ph is in the bone
Adult bone: dynamic, active and plastic
Coupled Bone Remodeling

Uncoupled = bone loss = osteopenia

Metra Biosystems
Fig. 21-4: Major hormones that regulate calcium metabolism. The parathyroid gland secretes the parathyroid hormone (PTH) which acts directly on bone to increase its resorption to mobilize calcium, thereby increasing (+) plasma calcium. Calcitonin from the thyroid gland inhibits bone resorption and lowers (-) plasma calcium. Calcitrol, a sterol derivative, increases calcium absorption from the intestine and decreases renal excretion. It also enhances bone resorption. Vitamin D3 is absorbed in the intestine or is formed in the skin under the influence of ultraviolet radiation. In the liver, vitamin D3 is converted to calcidiol, which in turn, is activated in the kidney to calcitriol, the most active form in calcium regulation.
Quality & Quantity

Bone Fragility

Histomorphology

Bone Geometry

Trabecular Architecture

Bone Mass (density)

Material Properties
- mineralization
- fatigue damage

Osteopenia

Osteoporosis (Fracture)
What causes bone loss and fragility?

“That’s not the kind of bone loss we talk about.”
Etiology of Bone Loss

- Postmenopausal (Type I) and
- Age-related (Type II)
- Type 1: mostly in women; estrogen deficiency, rapid with menopause, spine, wrist
- Type 2: men also, slow, many sites esp. hip
Age-related Bone Loss

- Senescence of osteoblasts (impaired function)
- Also increase in PTH levels (due to decrease renal and Ca re-absorption and intestinal Ca absorption that occurs in elderly - as less Vit D exposure, less synthesis of calcitrol, or vitD resistance?)
Fig. 21-3: Calcium metabolism. Note the different daily requirements of calcium with age; they almost double in women after 50, as compared to young adults.
Postmenopausal and Age-Related Bone Loss Integrated

- cannot look at bone loss in females without thinking of postmenopausal loss and life history
Multifactorial Etiology

• Number of factors that play a role in peak bone mass and loss:
  - Genetics and ethnicity
  - Lifestyle: alcohol, smoking, drugs
  - diet/nutrition
  - mechanical usage (physical activity)
  - reproductive factors (pregnancy, parity and lactation)

• Since multifactorial interest to look at its evolution and variation in different populations
Paleopathology and Osteoporosis

- The study of health and disease in the past = paleopathology
- Secondary Sources: documentary and iconographic data
- Primary Sources: skeletal remains
- Usually only direct evidence left in the archaeological record to examine health and disease in past populations
biocultural approach = emphasizes that environmental, cultural, and lifestyle factors have impact on the biology of disease.
OP in Past Populations

- Historical populations unique model to study bone loss
- Many studies of bone loss in various archaeological populations:
  - pattern of bone loss and fragility in the past is different than in clinical osteoporosis today
  - mostly bone mass
  - few studies of bone quality
  → trabecular architecture
Trabecular Architecture

Young normal

Elderly osteoporotic
Materials

- trabecular architecture
- several medieval British archaeological populations
- 4th lumbar vertebrae
- 3 adult age groups: 17-25, 26-45, 45+
Sample

- Wharram Percy
  - North Yorkshire, England
  - Burials represent primarily ordinary peasants
  - 11-16th centuries A.D.
Image Analysis

- trabecular architecture
- x-rays 5mm thick lumbar sections
- image processing and analysis, obtained binary and skeletonized images
Parameters

• **Structure:**
  trabecular bone volume (BV/TV), average trabecular thickness (Tb.Th), trabecular number (Tb.N), trabecular separation (Tb.Sp), and anisotropic ratio (Tb.An) (vertical:horizontal)

• **Connectivity:**
  Strut analysis: number of nodes/mm$^2$ (N.Nd) and termini/mm$^2$ (N.Tm), and terminus-to-terminus (Tm.Tm), node-to-terminus (Nd.Tm), and node-to-node (Nd.Nd) strut lengths (mm/mm$^2$), and (N.Nd/N.Tm).
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  **Connectivity:**
  2-D Star Volume (2D Star) strut analysis: number of nodes/mm² (N.Nd) and termini/mm² (N.Tm), and terminus-to-terminus (Tm.Tm), node-to-terminus (Nd.Tm), and node-to-node (Nd.Nd) strut lengths (mm/mm²), and (N.Nd/N.Tm).
Trabecular Structure:
Medieval - Rural

F M change by middle age; no 2 vs. 3

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<th>middle 30-49 yrs</th>
<th>old 50+ yrs</th>
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Strut Analysis

![Strut Analysis Diagram](image-url)
Connectivity: Rural

M decrease by middle age, no 2 vs. 3
F no difference between age groups
Modern Age--Related Change in Connectivity

Loss:
- accelerated post-menopause
- females > males

(Compston et al. 1987)
• fragility fractures greater in females
Medieval Results

• Both sexes: significant change in trabecular architecture by middle age
• No sex difference
• Low prevalence of fracture
• Different patterns than seen in modern populations
What is Going On?

RURAL Medieval Population

- Low life expectancy:
  - but infant mortality, longevity no change
- Problems with mortality samples:
  - secular trends: old age may not be comparable
  → may account for lack of typical “old age”
  but not lack of typical “post-menopause” fractures and bone loss
What is Going On?

- **Nutrition/diet:**
  - maybe sub-optimal conditions
  - no evidence for calcium or vitamin D deficiency
  - Vitamin D is likely important: Vitamin D insufficiency
  - Is Calcium really the big story in bone loss???
From Kanis (1994)
What is Going On?

- Physical activity:
  - rural farming population: both sexes involved in similar arduous activity
  - Could have protected both sexes from bone loss in old age
What is Going On?

→ Both diet and activity do not fully explain atypical patterns seen in females

• Reproductive Factors: pregnancy and lactation
Pregnancy and Lactation

- metabolically active states in bone
- bone loss during pregnancy
- long-term bone fragility? → unlikely
- With lactation recovery of bone loss
- Evolutionary perspective: reproduction should not be bad for skeleton
Nonhuman Primates

• plasticity in primate reproductive patterns

• our genetically closest primate relatives gorillas and chimps:
  → first birth soon after menarche
  → lactation 3-4 yrs with frequent nursing
  → ~5 offspring
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<tr>
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<td>• delayed first birth</td>
</tr>
<tr>
<td>• 3-4 years lactation</td>
<td>• little or no breast-feeding</td>
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<td>• family size of ~5</td>
<td>• average family size 2.5</td>
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<tr>
<td>• early menopause</td>
<td>• late menopause</td>
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**total # menstrual cycles:**

- 4 years (48 cycles)
- 35 years (420 cycles)

*After Sperling and Beyene (1997)*
Reproductive Behaviors
Rural Medieval vs. Modern

• extended lactation (maybe also wet nursing) and later age at weaning

• ↑parity (estimate 5-10 offspring)

• likely later menarche and slightly earlier menopause

= different hormonal environment
Discussion

Observation
- bone loss in young age
- lack of change middle and old age

Explanation?
- pre-menopausal women pregnant or lactating
- lower lifetime exposure to estrogen: less dramatic drop after menopause
Conclusions

- Skeletal remains offer unique evidence to study health and disease in past populations with a biocultural approach.
- Patterns of bone loss and fragility are different in the past than those seen in modern Western populations.
- Maybe due to lifestyle and layers of life history: reproductive factors.
Perspective

• Osteoporosis is a heterogeneous disorder: lifestyle factors clearly important
• Cannot understand female bone maintenance without considering role of reproductive patterns
• A combined biocultural, evolutionary and life history approach is vital to get at natural history of bone loss and fragility
• In taking this approach we improve our understanding of the disease today