Osteoporosis: The Definition

- Impaired bone strength
- Low BMD
- Poor bone quality
- Increased fracture risk due to bone loss
Osteoporosis

Bone Strength = Bone Qualities + Bone Density

Bone Qualities:
1. Micro-architecture
2. Turnover/stress
3. Damage
4. Matrix quality

Bone Density:
1. Size and geometry
2. Mineralization
Prevention of Osteoporosis
Non Pharmacological Approaches to the Prevention of Osteoporosis

- Adequate intake of dietary calcium
- Regular physical activity
- Minimize alcohol intake—1-2 small glasses/daily
- Encourage smoking cessation
- Minimize risk of fall
Your Mother Always Told You to Drink Your Milk... She Was Right!
Current Calcium Recommendations

- 1200 mg daily for women older than 50
- 1000 mg daily for men older than 50
- 1200 mg daily for men older than 70
- Try and obtain from food sources, then supplement
Calcium and MI Association?

- 2010 metanalysis showed possible assoc. btwn MI and >1500 mg of calcium daily
- However, recent study showed no assoc. btwn. calcium and inc. risk of MI
## Calcium Calculator

<table>
<thead>
<tr>
<th>Product</th>
<th>Servings / Day</th>
<th>Calcium (mg)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milk (8 oz.)</td>
<td>X 300</td>
<td>=</td>
<td></td>
</tr>
<tr>
<td>Yogurt (6 oz.)</td>
<td>X 300</td>
<td>=</td>
<td></td>
</tr>
<tr>
<td>Cheese (1 oz. or 1 cubic inch)</td>
<td>X 200</td>
<td>=</td>
<td></td>
</tr>
<tr>
<td>Fortified Foods / Juices</td>
<td>X 80-1,000</td>
<td>=</td>
<td></td>
</tr>
<tr>
<td>Estimated total from other foods</td>
<td></td>
<td>= 250</td>
<td></td>
</tr>
<tr>
<td>Total daily calcium intake, in mg</td>
<td></td>
<td>=</td>
<td></td>
</tr>
</tbody>
</table>
Which Type of Calcium?

- Calcium Carbonate—needs to be taken with food for best absorption
- Calcium Citrate—does not need to be taken with food
- Calcium Phosphate
- Calcium Gluconate
- Calcium Lactate
# Calcium Supplements

<table>
<thead>
<tr>
<th>Supplement Facts</th>
<th>Supplement Facts</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Serving Size:</strong> 2 tablets</td>
<td><strong>Serving Size:</strong> 1 tablet</td>
</tr>
<tr>
<td>Amount</td>
<td>% Daily Value</td>
</tr>
<tr>
<td>Calcium (as calcium citrate)</td>
<td>400 mg</td>
</tr>
</tbody>
</table>

[Supplement Facts Image]
Vitamin D

• Vitamin D is added to milk and OJ and is in liver and fatty fish.

• You can get vitamin D from the sun. But, you need sunscreen to protect your skin which also blocks vitamin D.

• To get enough vitamin D, many people need to take a supplement.
Vitamin D

- 800-1000 IU daily
- Max. dose recommended: 4000 IU daily
- Recent studies show no association with cardiovascular disease or reduction in breast cancer
Exercises for Osteoporosis

- **Shoulder blade squeeze**
  - To stretch your chest and strengthen your upper back muscles:
  - With your feet flat on the floor, sit slightly forward in a sturdy chair, keeping your back and neck straight.
  - Look straight ahead, bending your arms at the elbows (1).
  - Gently move your elbows and shoulder blades back as far as you can and still be comfortable (2).
  - Hold the position for five seconds while breathing normally. Return your arms to the starting position. Repeat this exercise five to 10 times, depending on your ability.
Weight-bearing Exercises

• Which exercise is for you?
  
  - **Low impact**: walking, elliptical, low impact aerobics, stair-stepper, tai chi

  - **High impact**: jogging or running, aerobic dancing, hiking, jumping rope, stair climbing
Weight-bearing Exercises

• Which exercise is for you?
  – Try to do the exercises with greatest impact that do not cause problems

• Try to do 30 minutes of weight-bearing exercise, at a moderate pace, most days of the week
Muscle-strengthening Exercises

• Muscle-strengthening exercises make you move your body, a weight or some other resistance against gravity

• Some options include:
  – Lifting weights (machines or free weights)
  – Calisthenics (partial or full push ups, wall slide/wall sits, prone trunk lifts)
  – Using exercise bands or tubes
Fall Prevention

• Have your eyes checked
• Have your medications checked
• Stay active and do weight bearing exercise
• If needed use walker, cane or other source to help prevent falls
• Ask you doctor about physical therapy
Fall Prevention in the Home

- Use handrails on stairs, in bathrooms
- Keep floors clutter-free
- Keep floors clean but not slippery
- Place skid-proof backing on carpets and rug
- Use rubber mat in shower/tub
- Use 100 watt bulbs in all rooms
- Install ceiling lighting in bedrooms
What About Caffeine?

- Coffee—calcium intake with coffee
- Tea—?evidence
- Soda—Cola—Tufts study showed phosphoric acid did cause significant bone loss
Alcohol and Tobacco

- Minimize ETOH use to <2 glasses daily
- Smoking cessation is key to healthy bones
Therapies for Osteoporosis
FDA Approved Therapies for Osteoporosis

- Bisphosphonates
  - Alendronate
  - Risedronate
  - Ibandronate
  - Zolendronic Acid
- Raloxifene
- Denosumab
- Teripartide - formation

- Life style modifications
  - Calcium and vitamin D
  - Weight bearing exercises
  - Fall prevention
Treatment Objectives

**Osteoclast**
- Inhibition of resorption

**Osteoblast**
- Stimulation of formation
Bisphosphonates

- Work by inhibiting osteoclast function
- Oral and IV forms
- Side effects:
  - Renal impairment
  - Rash
  - Esophagitis
  - Osteonecrosis of the Jaw
Atypical Femur Fracture

- Located at diaphyseal area
- Lateral cortical thickening
- Transverse Fracture with short oblique extension medially (beaking)
- Often Bilateral
- More common in Asians, prior bisphosphonate use
- Occur with longer term use >5-10 years
X-rays showing an impending femoral shaft fracture (A) and a representative atypical diaphyseal femoral fracture (B) with thickened cortices and a beak or spike. [Courtesy of J. Lane and A. Unnanuntana, Hospital for Special Surgery, New York, NY.].

Watts N B, Diab D L. JCEM 2010;95:1555-1565
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## Duration of Bisphosphonate Treatment

<table>
<thead>
<tr>
<th>Patient’s fracture risk</th>
<th>Suggested duration of treatment</th>
<th>Suggested duration of drug holiday&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>Treatment rarely indicated</td>
<td>NA</td>
</tr>
<tr>
<td>Mildly increased</td>
<td>Treat for approximately 5 yr</td>
<td>Stay off bisphosphonate until BMD decreases significantly or fracture occurs</td>
</tr>
<tr>
<td>Moderately increased</td>
<td>Treat for 5–10 yr</td>
<td>Stay off bisphosphonate for 2–3 yr (or less if BMD decreases or fracture occurs)</td>
</tr>
<tr>
<td>High</td>
<td>Treat for 10 yr</td>
<td>Stay off bisphosphonate for 1–2 yr (or less if BMD decreases or fracture occurs); alternate medication (e.g. raloxifene, teriparatide) may be given during the holiday from bisphosphonates</td>
</tr>
</tbody>
</table>

Duration is based largely on personal opinion.

<sup>a</sup> Longer holidays might be appropriate for patients treated with bisphosphonates that bind most strongly to bone (i.e. zoledronic acid, alendronate), whereas shorter holidays might be considered for patients treated with compounds that bind less strongly (i.e. risedronate, ibandronate).
Raloxifene (Evista)
Effects of Raloxifene on New Vertebral Fractures: The MORE Trial—36 Months

% of Patients With Incident Vertebral Fracture

- Placebo
- 60 mg/d of raloxifene
- 120 mg/d of raloxifene

RR, 0.5 (95% CI, 0.4-0.6)
RR, 0.7 (95% CI, 0.6-0.9)
RR, 0.6 (95% CI, 0.4-0.9)
RR, 0.5 (95% CI, 0.3-0.7)

*Not FDA-approved dose

Effects ofRaloxifene on Nonvertebral Fractures
The MORE Trial—36 Months

Osteoporotic Nonvertebral Fractures

Hip Fractures

% of Patients With Incident Nonvertebral Fracture

0 5 10 15
0 1 2 3

0 6 12 18 24 30 36
0 6 12 18 24 30 36

Placebo  Pooled raloxifene doses

RALOXIFENE

- FDA approved for treatment of osteoporosis in postmenopausal women
- Reduced risk of new vertebral fractures by about 55% and 30% in women with prior vertebral fractures
- Did not reduce fracture risk in hip and nonvertebral in clinical trials
- Increased risk of DVT, hot flashes, and CVA in high risk populations
Denosumab

- Human monoclonal antibody
- Binds to Rank-L and prevent it from binding to RANK
- Action: inhibits osteoclasts
- Works like OPG
Regulation of Osteoclastogenesis by Factors from Osteoblast / Stromal Cells

Freedom Trial

- Randomized, placebo-controlled trial
- 60 mg of Denosumab SQ every 6 months for 3 years
- Reduced vertebral fracture risk by 68%
- Reduced hip fractures by 40%
- Reduced nonvertebral fractures by 20%
Side Effects of Denosumab

- Increased skin infections: cellulitis, erysipelas
- Over-suppression of the bone
- Atrial fibrillation, ONJ, and mortality were similar in placebo group and treated group
Teriparatide [rDNA Origin] Injection
FORTEO®
Parathyroid Hormone (PTH) – Mechanism of Action

**PTH binds to cell surface G protein-coupled receptor**

- **Decreased apoptosis of osteoblasts**
- **Stimulates differentiation of bone lining cells and preosteoblasts to osteoblast**

**Net increase in number and action of bone forming osteoblasts**
Teriparatide Indications

- Previous Fragility Fracture in postmenopausal women and men
- T score: -3.0 without fracture
- Cannot tolerate another therapy
- Bone loss or fracture on another therapy
Teriparatide

- The teriparatide Pen is a prefilled delivery device that can be used up to 4 weeks (28 daily doses)
- Dose: 20 mcg once daily
- Administered as a subcutaneous injection into the thigh or abdominal wall
- Duration of therapy: 18-24 months
Effect of Teriparatide on Incidence of Vertebral and Nonvertebral Fractures in Postmenopausal Women With Osteoporosis

New Vertebral Fracture

- Placebo: 14%
- 20 μg PTH: 65%

Nonvertebral Fractures

- Placebo: 16%
- 20 μg PTH: 53%

P < 0.01

Side Effects of Teriparatide

- Mild transient increase in serum calcium
- Mean increase in urine calcium of 30 mg in 24 hrs
- Leg cramps
- Dizziness
- Black Box warning--↑ incidence of osteosarcoma with high dose longer-term exposure
- Transient tachycardia/HTN after 1st dose
FORTEO® (Teriparatide [rDNA Origin] Injection)
Important Safety Information

Warning

In male and female rats, teriparatide caused an increase in the incidence of osteosarcoma (a malignant bone tumor), that was dependent on dose and treatment duration. The effect was observed at systemic exposures to teriparatide ranging from 3 to 60 times the exposure in humans given a 20 mcg dose. Because of the uncertain relevance of the rat osteosarcoma finding to humans, teriparatide should be prescribed only to patients for whom the potential benefits are considered to outweigh the potential risk. Teriparatide should not be prescribed for patients who are at increased baseline risk for osteosarcoma (including those with Paget’s disease of bone or unexplained elevations of alkaline phosphatase, open epiphyses, or prior external beam or implant radiation therapy involving the skeleton) (see WARNINGS and PRECAUTIONS, Carcinogenesis)
Contraindications to Forteo

- Paget’s disease/↑ alkaline phosphatase
- History of radiation to bone
- Open Epiphyses
- Primary or Metastatic skeletal malignancy
- Hypercalcemia or increased PTH
- Pregnancy/lactation
- Renal insufficiency
### New Therapies

<table>
<thead>
<tr>
<th></th>
<th>Cathepsin-K Inhibitor</th>
<th>Currently in Phase III Clinical Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Odanacatib</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Romosozumab</strong></td>
<td>anti-sclerostin abs</td>
<td>Currently in Phase III Clinical Trials</td>
</tr>
<tr>
<td><strong>PTHrp</strong></td>
<td></td>
<td>Phase III Clinical Trials</td>
</tr>
</tbody>
</table>
Romosozumab

- 12 month phase II trial data showed when given every month significant improvements in BMD—more than other medications
- Bone formation!
Romosozumab

Figure 1. Study Schema to 12 Months.
Alendronate and teriparatide were administered in an open-label fashion, whereas the administration of placebo and the various romosozumab doses was blinded.
**Romosozumab**

![Graphs showing percentage change from baseline in bone mineral density](image)

**Figure 2. Percentage Change from Baseline in Bone Mineral Density.**

Data are least-squares means, and I bars indicate 95% confidence intervals. The asterisk indicates $P<0.05$ for the comparison of the 210-mg monthly dose of romosozumab with placebo, the dagger $P<0.02$ for the comparison of the 210-mg monthly dose with alendronate, and the double dagger $P<0.02$ for the comparison of the 210-mg monthly dose with teriparatide.
Any Questions or Comments?

Will Your Bones Last As Long As You Do?
Bone Health Education and Support Group

Join us each month for informative presentations by leading experts about the latest discoveries in the prevention, diagnosis and treatment of osteopenia and osteoporosis. You will have the opportunity to ask these experts questions and to talk with others who share your interest in bone health.

San Diego Osteoporosis Education and Support Group
1st Wednesday of every month
Noon
Thornton Hospital, 3rd floor
SDG&E Room 3-102
All meetings are free and open to the public.

The mission of the National Osteoporosis Foundation San Diego Support Group is to meet regularly and offer education, information, encouragement and support to people who are affected by osteoporosis and/or osteopenia, or would like to learn more about osteoporosis.

The group is an affiliate of the National Osteoporosis Foundation (NOF), and has pledged to support the organization’s goals of: (1) providing accurate, up-to-date osteoporosis information to patients, as well as to family members and caregivers, as appropriate; and (2) creating opportunities for affected persons to share concerns, problems and coping strategies with the goal of better managing their condition.

For questions or to RSVP, please contact Heather Hofflich, DO, at hhofflich@ucsd.edu or 858-657-7236.
Thank You