DEFINITIONS
Osteoporosis is a systemic skeletal disease characterized by low bone mass and micro-architectural deterioration of bone tissue, resulting in reduced bone strength and increased risk of fracture.

EPIDEMIOLOGY
- 44 million adults in the US have abnormally low bone mass
- 40% of all women and 25% of all men will experience a fragility fracture in their lifetime.
- Osteoporosis accounts for 800,000 vertebral compression fractures, 300,000 hip fractures and 250,000 wrist fractures annually.
- The consequences of those fractures are significant: the mortality for hip fracture is 24% in the first 12 months; of those who survive, 50% fail to regain full ambulatory capability.
- Vertebral fractures can be asymptomatic but they can also be associated with back pain, reduced activity, and increased mortality.
- Under-diagnosis and under-treatment are common.

PRINCIPAL RISK FACTORS FOR OSTEOPOROSIS AND FRAGILITY FRACTURES
- Personal history of a prior fragility fracture is the strongest predictor of a subsequent fracture regardless of bone density.
- Low weight.
- Female gender.
- Advancing age.
- History of falls and unsteady gait.

ETIOLOGY
- Primary osteoporosis is associated with many factors, including nutrition, low peak bone mass, genetics, low level of physical activity and early menopause. Postmenopausal osteoporosis is by far the most common form of osteoporosis. Bone remodeling is lifelong; however, increased bone resorption after age 30 results in net bone loss, most rapidly during the first 5 years following menopause.
- Secondary osteoporosis (Table 1).

SYMPTOMS
- Often silent. The prevalence of osteoporosis is 38% in white women aged 70 to 79 and 70% in those aged above 80. This means that osteoporosis should be presumed to exist in all elderly women until proven otherwise.
- The most common sign of osteoporosis is height loss. Elderly patients should be measured yearly.
- Another sign is thoracic kyphosis (dowager’s hump).
- Osteoporosis without fractures does not cause pain.

WORK-UP
- Diagnosis of osteoporosis is made by bone densitometry, indicated in:
  - All women 65+ and women under age 65 with osteoporosis risk factors.
  - All adults with fragility fractures.
  - Anyone expected to be treated with glucocorticoids for longer than 3 months or with diseases associated with secondary osteoporosis.
  - Men 70 and older (controversial).

TECHNOLOGIES FOR MEASURING BONE MINERAL DENSITY (BMD)
- Quantitative ultrasound (QUS) should be used only for screening in low osteoporosis prevalence populations.
- Dual-energy x-ray absorptiometry (DXA) is the “gold standard” because epidemiologic studies have correlated and standardized BMD data obtained by DXA with fracture risk. However, any dense structure between radiation source and film (e.g., osteophytes or vascular calcifications) will give a falsely high reading, because density is measured from a 2-dimensional image.
- Quantitative computed tomography (QCT) measures the intended 3-dimensional targeted bone only.

INTERPRETATION
All BMD results are measured in gm/cm², but expressed in T scores and Z scores. T scores are standard deviations (SDs) above or below values for young normal adults and Z scores are standard deviations above or below age-matched values. A T score more than 2 SDs below the mean 30-year-old BMD indicates an increased risk of fracture and should lead to therapy to prevent further bone loss. A Z score of more than 1 SD below the age-matched mean value signifies a BMD that is lower than expected for one’s age and should prompt an evaluation for secondary causes of bone loss.

WORLD HEALTH ORGANIZATION CRITERIA FOR THE DIAGNOSIS OR OSTEOPOROSIS

<table>
<thead>
<tr>
<th>T-score</th>
<th></th>
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<tbody>
<tr>
<td>Normal</td>
<td>&gt;-1</td>
</tr>
<tr>
<td>Osteopenia (or low bone mass)</td>
<td>-1 to -2.5</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>≤-2.5</td>
</tr>
</tbody>
</table>

The work-up for secondary causes of osteoporosis is presented in Table 1.
The goal of treatment is fracture prevention. The strongest predictors of fracture are previous fracture(s), fall(s), low BMD and advancing age.

Nonpharmacologic Management
- Resistive exercises
  - walking
  - rowing machine
  - weight lifting
- Fall prevention
  - assess gait and fall risk (e.g., "get up and go" test)
  - gait training
  - home safety evaluation
  - assistive devices as appropriate
- Hip protectors
- Supplements
  - calcium
  - provide 1,500 mg per day from diet and/or supplements
    - examples of dietary sources include:
      - milk = 300 mg per 8 oz
      - yogurt = 350 mg per cup
      - broccoli = 100 mg per cup
      - seaweed = >1000 mg per serving
  - supplements
    - calcium carbonate
    - calcium citrate

Vitamin D plays an important role in calcium homeostasis and bone metabolism. Low levels of vitamin D lead to inadequate intestinal calcium absorption and result in relative hypocalcemia triggering secretion of parathyroid hormone (PTH). PTH stimulates osteoclastic activity and calcium release from bone to maintain eucalcemia at a cost of loss in bone mass.10,11

To become biologically effective, nutritional vitamin D and skin-synthesized vitamin D must be hydroxylated twice: first in the liver to become 25 (OH) vit D, then in the kidney to become 1-25 (di-OH) vit D. Adequacy of vit D stores is best measured by the serum levels of 25 (OH) vit D, except in patients with renal failure in whom 1-25 (di-OH) vit D should be measured.

Vit D deficiency is defined by a level of 25 (OH) vit D < 10 ng/ml; however, secondary hyperparathyroidism occurs at a level of 25 (OH) vit D < 30 ng/ml (vit D insufficiency), which is the threshold for optimum bone health.

The prevalence of low vit D level is high; NHANESIII data show that 32% of Caucasians, 55% of Mexican-Americans and 67% of African-Americans over age 50 have 25 (OH) vit D level < 23 mg/ml. Such numbers could justify population-wide screening for vit D deficiency. Among patients with low UV-B sunlight exposure (e.g., nursing home patients), the prevalence of vit D deficiency is even higher.12

In addition to bone health, vit D deficiency has been associated with muscle weakness, falls, myalgias, fibromyalgia, several cancers (colon, breast, prostate), hypertension, rheumatoid arthritis and even type I diabetes mellitus.
The daily requirement of vit D in the geriatric population is at least 800 units per day. Vit D3 is more effective than D2, but either type will do the job. In patients whose level of 25 (OH) vit D is < 30 ng/ml, a weekly dose of vit D 50,000u orally for 2 months is appropriate. Once the 25 (OH) vit D level has been replenished to > 30 ng/ml, the daily requirement of 800 units should be prescribed indefinitely. Note that all the trials of pharmacologic agents used to treat osteoporosis have been conducted in calcium and vit D replete subjects.

**Pharmacologic Treatment**

- Preventive treatment for osteoporosis and treatment of osteopenia are controversial, even though some drugs have FDA approval for prevention.
- Indication for treatment (according to the National Osteoporosis Foundation):
  1. T-score < -2.0 (by central DXA)
  2. T-score < -1.5 (by central DXA) plus at least one additional fracture risk factor
  3. Any prior history of fragility fracture: such patients should be treated even if a DXA is not available (e.g. nursing home residents).
- Antiresorptive (i.e., anti-osteoclastic) treatments
  - estrogen: conjugated estrogen 0.625 mg daily is efficacious in preventing fractures; however, the overall risk outweighs the benefit. This treatment is no longer recommended for osteoporosis.
  - selective estrogen receptor modulators (SERMs): raloxifén 60 mg daily is approved for the treatment (and prevention) of osteoporosis. It is efficacious in reducing the risk of vertebral fractures and reduces the risk of breast cancer. Side effects are hot flashes, leg cramps, and increased risk of deep vein thrombosis and endometrial cancer.
  - calcitonin nasal spray 200 IU per day reduces the risk of vertebral fractures. The drug is well tolerated, but probably less effective than other agents.
  - bisphosphonates

Three bisphosphonates are widely used for the treatment or prevention of osteoporosis as first line agents. They are alendronate (70 mg p.o. weekly or 10 mg p.o. daily),17,18 risedronate (35 mg p.o. weekly or 5 mg p.o. daily)19,20 and ibandronate (150 mg once monthly or 2.5 mg daily). All three drugs are efficacious in reducing fractures. Side effects of these drugs include esophageal ulceration, musculoskeletal pain and diarrhea. Any co-administered substances (food or medication) binds to bisphosphonates which must be taken fasting with 8 oz of water and trunk upright. Nothing else is contraindicated.

Markers of bone turnover can be used to monitor treatment. The most common markers of bone resorption include hydroxyproline and N-telopeptide. The most common markers of bone formation are alkaline phosphatase and osteocalcin. Change in those markers often occurs within three months of effective treatment, but they correlate poorly with fracture risk.

**Duration of Treatment**

Treatment trials were not conducted for periods longer than 5 years. Some clinicians hesitate to treat for longer than 5 years (for lack of any evidence base), while others treat indefinitely because BMD declines after treatment withdrawal.

**Osteoporosis in Men**

Twenty percent of all osteoporotic persons in the US are men. Secondary causes (e.g., hypogonadism) are more likely than in women, who typically have primary osteoporosis. Bisphosphonates, calcitonin and teriparatide are used to treat osteoporotic men.

**References**

Disclosure of Financial Interests
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