Role of Bone Scanning in Asthma and Osteoporosis

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Tampa Florida
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- Definition
- Epidemiology
- Risk Factors
- Asthma and Osteoporosis
- Corticosteroids and Osteoporosis
- Laboratory Evaluation
- Prevention
Role of Bone Scanning in Asthma and Osteoporosis

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- Assessing bone density
- Treatment
- Side Effects of Treatment
- Preventing osteoporosis in patients on systemic high dose glucocorticosteroids
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Definition of Osteoporosis

- A disease characterized by low bone mass and microarchitectural deterioration of bone tissue, leading to enhanced bone fragility and a consequent increase in fracture risk.
- Decrease of T score by < 2.5 standard deviations (T score compares individual to idealized young subject or peak bone mass).
Low-power scanning electron micrograph of trabecular bone

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Epidemiology of Osteoporosis

- 40% of white women > 45 years of age
- 15% of white men > 50 years of age
- 1.5 million fractures/year in US
  - 1.7 million hip fractures/year worldwide 1990
  - 6.3 million hip fracture/year worldwide 2050
- One-third of subjects with hip fracture become totally dependent
- Estimated 10-24% excess death rate after hip fracture after age 50
DEXA Scans
More Than 2.5 SD Decrease in T Score

- 2% US women 30-50 years of age
- 15% US women 50-60 years of age
- 31% US women 60-70 years of age
- 44% US women 70-80 years of age
- 48% US women > 80 years of age
- Fracture rate doubles for every SD decrease in T score
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Risk Factors for Osteoporosis

- Age > 60 years
- Female gender
- Oriental > Caucasian > African-American
- Diet deficient in calcium
- Low body mass
- Minimal weight bearing exercise
Risk Factors for Osteoporosis

- Positive family history
- Life style issues (smoking, EtOH)
- Infertility (premature oophorectomy)
- Menopause (especially premature)
- Endocrine disorders
- Medications
- Inflammatory diseases
Women With Osteoporotic Fractures Often Go Undiagnosed and Untreated


% of patients with osteoporotic fracture not investigated or treated:
- No BMD before index fracture
- No BMD after index fracture
- No osteoporosis diagnosis
- No calcium prescribed
- No vitamin D prescribed
- No bisphosphonate prescribed

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Asthma and Osteoporosis

- Asthma may be an independent risk factor but data are controversial.

Also:

1. corticosteroids
2. ↓ mobility

Iqbal et al. Chest 1999:116;1616
COPD and Osteoporosis

• Studies support the hypothesis that COPD is an independent risk factor.

Also:

1. corticosteroids
2. body mass index
3. smoking
4. ↓ mobility
5. hypogonadism

Iqbal et al. Chest 1999:116;1616
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Effects of Corticosteroid Therapy on Bone Metabolism

- Decreased growth hormone secretion
- Decreased protein synthesis
- Decreased GI absorption of calcium
- Secondary increased PTH secretion
- Decreased Vitamin D activation
- Decreased sex hormone production
- Increased calcium excretion
- Decreased osteoblast and increased osteoclast activity
Truths About Corticosteroid Therapy and Osteoporosis

• Inhaled corticosteroid Rx is safer than systemic

• Some individuals are at greater risk than others (risk factors for osteoporosis may help to identify some)

• Various ICS differ in effects on bone but safest is unknown
Myths About Corticosteroid Therapy and Osteoporosis

- “low dose” systemic Rx is safe
- Every other day systemic Rx is safe
- Bone effects require long term Rx
- Topical CS (ICS) Rx has no systemic side effects
Corticosteroids and Osteoporosis

- 7.5 mg prednisone/day decreased bone density 3%/year
- < 10 mg prednisone/day decreased bone density of the spine by 10-12%
- Systemic CS administered qod does not spare bone
- Most rapid loss occurs in first 6-12 months
Risk Factors for Osteoporosis Associated with ICS Rx

- Dose
- Specific corticosteroid
- Technique of administration
- Duration of Rx
Stratify Risk of Osteoporosis
Inhalational Corticosteroids

- Low risk
  - ICS $\leq 0.8-1$ mg/day for adults
  - ICS $\leq 0.4-0.5$ mg/day for children
  - Include nasal ICS
  - No other risk factors other than ICS
Stratify Risk of Osteoporosis

- Moderate risk
  - ICS > 0.8-1.0 mg/day for adults
  - ICS > 0.4-0.5 mg/day for children
  - Include nasal ICS
  - May have one other risk factor
Stratify Risk of Osteoporosis

- High risk
  - Chronic systemic CS
  - Systemic CS > 4 weeks continuously
  - Systemic CS bursts ≥ 4 per 12 months
Do Inhaled Steroids Increase the Risk of Osteoporosis?

- Evidence-based answer:
  1) Conventional doses for asthma are not associated with significant bone loss at 2 to 3 years follow-up (strength of recommendation: A)
  2) Higher doses may be associated with negative bone density changes in up to 4 years: C
  3) Evidence lacking on whether nasal steroids increase risk.
  4) Longer-term studies are necessary

Prospective Trial of BCM or BUD (JACI 1995;96:157)

- Decrease 0.5 SD Z score per 1 mg ICS/day
- Paradoxical increase in bone density and decrease in fracture rate with duration of Rx
- No increased risk in postmenopausal women (all received estrogen)
- Prevalence of vertebral fracture decreased with cumulative lifetime inhaled dose
- High variability unexplained by CS Rx

BCM = beclomethasone; BUD = budesonide
ICS Effects on Bone Density of Premenopausal Women (NEJM 2001;345:941-7)

- 109 premenopausal women, 18-45 years of age, treated with inhaled triamcinolone
- 3 year study
- 0.00044 g/cm² reduction at hip per puff (100 mcg) / year; no change in spine and femoral neck
Children and Osteoporosis

- No reduction in bone density 0.65-1 mg/d
  - Toogood 1996
- Decrease (not statistical) in gain of bone density with maturation
  - Eur Respir J 1994;7:710-714
- Growth rate affected by 0.6-0.8 mg/day
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Biochemical Markers of Bone Metabolism

- Serum indicators of bone resorption
  - C-telopeptide of type I procollagen
  - cross-linked N-telopeptide of type I collagen
  - deoxypyridinoline crosslinks
- Urine indicators of bone resorption
  - hydroxylysine or hydroxyproline
- Serum indicators of bone formation
  - bone-specific alkaline phosphatase
  - Osteocalcin
  - Carboxy terminal propeptide type I collagen
Medical Evaluation of Osteoporosis

- Serum calcium, creatinine, phosphorus, alkaline phosphatase, transaminases
- TSH
- Estradiol level if premenopausal with irregular menses
- Free testosterone in men
- 24 hour urine for calcium and creatinine
- 25-OH Vitamin D and PTH level
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Adequate Calcium and Vitamin D Intake for Everyone

- Advise all individuals to obtain an adequate intake of dietary calcium including supplements if necessary (safe upper limit for total calcium intake set at 2500 mg/day), and vitamin D, 800 IU per day for all individuals (safe upper limit for vitamin D is 2000 IU/day). (1-3 yr, 500 mg/day; 4-8 yr, 800 mg/day; 9-18 yr, 1300 mg/day; 19-49 yr, 1000 mg/day; > 50 yr, 1200 mg/day)

- Vitamin D, 800 IU or more per day for those at risk of deficiency, i.e., elderly, chronically ill, housebound, institutionalized.
Calcium Intake from Calcium Rich Foods*

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<tr>
<th>Product</th>
<th>Calcium content per serving, mg</th>
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<tr>
<td>Milk (8 oz)</td>
<td>300</td>
</tr>
<tr>
<td>Yogurt (8 oz)</td>
<td>400</td>
</tr>
<tr>
<td>Cheese (1 oz)</td>
<td>200</td>
</tr>
<tr>
<td>Fortified Foods or Juices</td>
<td>80 – 1000**</td>
</tr>
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* About 75% to 80% of the calcium consumed in the American diets is from dairy products.

** Calcium content of fortified foods varies.

Post-menopausal American women consume ~ 600 mg/day CA.
Vitamin D Enriched Foods

Vitamin-D-fortified milk (400 IU per quart)
Cereals (40 to 50 IU per serving)
Egg yolks
Salt-water fish
Liver

Best assurance of adequate vitamin D is a multi-vitamin with 400, or more, IU.
Regular Weight-Bearing Exercise

- Recommend regular weight-bearing and muscle-strengthening exercise to reduce the risk of falls and fractures.

Avoidance to Protect Against Osteoporosis

- Avoid tobacco smoking
- Avoid excessive alcohol intake
Strategies to Minimize Osteoporosis

- Discontinue systemic CS
- Lower dose of ICS
- Divide dose of ICS
- Use ICS sparing agent
- Exclude other Dxs which complicate or emulate asthma
- Increase awareness of osteoporosis
- Recognize, diagnose and Rx osteoporosis
Conclusions

1. As population ages, so too will the incidence of osteoporosis.
2. Risk factors are many including all glucocorticosteroids.
3. Subjects with asthma, because of sedentary life and glucocorticosteroids, predisposed to osteoporosis.
4. Laboratory evaluation necessary, especially in cases of early onset.
5. Dietary history and sun exposure important.
6. Prevention is the name of the game.
Thank you!
Methods to Assess Bone Density or Bone Metabolism

- Dual energy X-Ray absorptiometry (DEXA)
- Single energy X-Ray absorptiometry
- Quantitated CT
- Ultrasound
- Plain radiographs
- Biochemical markers
- Bone biopsy
Dual Energy X-Ray Absorptiometry (DEXA)

- Preferred method of bone density assay
  - least cost
  - most accurate
  - less radiation exposure
- Precision of current instruments 1-3%
  - change > 2.8 X precision, 95% confidence interval
- Precision affected by marrow fat and anatomy of spine
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Kearney DM, Lockey RF. *Ann Allergy Asthma Immunol* 2006;96:769-776
# Medications for the Prevention and Treatment of Osteoporosis

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<td>0.625 mg orally once a day</td>
<td>Increased risk of pulmonary emboli, myocardial infarction, strokes, breast cancer</td>
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<td>estrogen</td>
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<td>Bisphosphonates: ibandronate (Boniva),</td>
<td>150 mg once a month, 35 mg orally once a week</td>
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Kearney DM, Lockey RF. *Ann Allergy Asthma Immunol*
Initiate therapy to reduce fracture risk with:

- BMD T-scores below –2.5 by central DXA with no risk factors
- BMD T-scores below –2.0 by central DXA with one or more risk factors
- A history of a prior vertebral or hip fracture
Bisphosphonates

- Alendronate (Fosamax®), risedronate (Actonel®), and ibandronate (Boniva®) are approved for use in osteoporosis.
- Bisphosphonates are classified as antiresorptive medications.
- Bisphosphonates bind to hydroxyapatite crystals in bone and osteoclast-bone interface, inhibiting osteoclast activity.
- Bisphosphonates inhibit resorption of bone and lead to increases in bone density and reduced fracture risk.
Alendronate (Fosamax®) approved for prevention (5 mg daily and 35 mg weekly) and treatment (10 mg daily and 70 mg weekly) of osteoporosis for postmenopausal women. 3-year treatment increases bone mass and reduces vertebral, hip, and non-vertebral fractures by 50%.
Long-Term Effect of Alendronate on BMD in Postmenopausal Women With Osteoporosis

Effect of Once-Weekly Alendronate in Postmenopausal Women With Osteoporosis


10 mg once daily (n=370)
35 mg twice weekly (n=369)
70 mg once weekly (n=519)

*All changes were significant increases from baseline (P <0.05).

• Risedronate (Actonel®) approved for prevention (5 mg dose and 35 mg weekly) and treatment of postmenopausal osteoporosis. Controlled trails indicate risedronate increases bone mass and reduces risk of vertebral fractures by 40% and all non-vertebral fractures by 30% over 3 years.
Effect of Risedronate on Hip Fracture Risk in Women 70-79 Yrs. of Age With PMO

*RR=0.6, 95% CI=0.4-0.9.

• Ibandronate (Boniva®) 150 mg by mouth once-a-month.

• Effectiveness, precautions, and side effects are similar to other bisphosphonates.
Side Effects and Administration of Bisphosphonates

- Few side effects versus placebo except for dysphagia, esophagitis, and esophageal or gastric ulcer

- Therefore, both taken after prolonged fast with 8 ounces of water (no other liquid approved) at least 30 minutes before eating and drinking

- Patient should remain upright during interval
Calcitonin (Miacalcin®)

- Approved for treatment of osteoporosis in women at least 5 years postmenopausal
- 200 international units (IU) delivered intranasally
- Subcutaneous (SC) also available
- Trials indicate decreased vertebral fracture rate by 54%
- Another trial indicated lower vertebral fracture rate by 21%
- Did not alter non-vertebral fracture rate
- Side effects safe and, rarely, epistaxis
Intranasal Salmon Calcitonin: 5-Year Results of the PROOF Trial

*P <0.05 vs. placebo.

Estrogen/Hormone Therapy (ET/HT)

- HT (Prempro®) reduced clinical vertebral and hip fractures by 34%
- FDA recommends that when used solely to prevent osteoporosis, approved non-estrogen treatments should be first carefully considered
- Women without hysterectomy require HT which contains progestin to protect uterine lining
- ET/HT should be used in lowest possible doses for the shortest duration to meet treatment goals
Parathyroid Hormone [PTH (1-34)]

Brand name: Forteo®

- Approved to treat osteoporosis in postmenopausal women
- PTH is an anabolic (bone-building) agent administered by subcutaneous route
- Decreases vertebral and non-vertebral fractures by 65% and 54%, respectively, after ~ 18 months
- Side effects: leg cramps and dizziness
- Patients at risk for osteosarcoma (Paget’s disease, prior radiation therapy of skeleton, bone metastases, hypercalcemia, history of skeletal malignancy) should not receive PTH therapy
Effect of PTH on Fracture Risk in Postmenopausal Women

- Placebo
- 20 µg PTH
- 40 µg PTH

* RR=0.35, 95% CI=0.22-0.55.
† RR=0.31, 95% CI=0.19-0.50.
‡ RR=0.47, 95% CI=0.25-0.88.
§ RR=0.46, 95% CI=0.25-0.86.

Raloxifene

Brand name: Evista®

- Approved for prevention and treatment of osteoporosis in postmenopausal women
- Increases vertebral bone mass modestly and reduces risk of vertebral fracture by 40%
- No evidence reduces risk of non-vertebral fractures
- Increases risk of deep vein thrombosis similar to estrogen
- Also increase hot flashes (~6% over placebo)
Effect of Raloxifene on Incident Vertebral Fractures in Postmenopausal Women With Osteoporosis

Placebo (n=2292)
60 mg/d raloxifene (n=2259)
120 mg/d raloxifene (n=2277)

* RR=0.5, 95% CI=0.3-0.7.
† RR=0.6, 95% CI=0.4-0.9.
‡ RR, 0.7, 95% CI=0.6-0.9.
§ RR, 0.5, 95% CI=0.4-0.6.

Combination Therapy

- Combination therapy may provide additional small increases in BMD, but controversial

- Added cost versus potential side effects should weighed against potential gains
Patient beginning therapy with glucocorticoid (prednisone equivalent of 5 mg/day) with plans for treatment duration of 3 months:

- Modify lifestyle risk factors for osteoporosis
- Smoking cessation or avoidance
- Reduction of alcohol consumption if excessive
- Instruct in weight-bearing physical exercise
- Initiate supplementation with vitamin D (plain or activated form)
- Prescribe bisphosphonate (use with caution in premenopausal women)

ACR Committee on GCS – Induced Osteo. Arthritis & Rheumatism 2001;44:1496-1503
Patient receiving long-term glucocorticoid therapy (prednisone equivalent of 5 mg/day):

- Same as previous slide
- Prescribe treatment to replace gonadal sex hormones if deficient or otherwise clinically indicated
- If BMD is not normal (i.e., T-score below –1) then
  - Prescribe bisphosphonate (use caution in premenopausal women)
  - Consider calcitonin as second-line agent if patient has contraindication to or does not tolerate bisphosphonate therapy
- If BMD is normal, follow-up and repeat BMD measurement either annually or biannually

ACR Committee on GCS – Induced Osteo. Arthritis & Rheumatism 2001;44:1496-1503
Conclusions

- All patients are at risk for osteoporosis: \( \text{♀} > \text{♂}; \) older > younger; those with risk factors versus those with none; COPD and asthma > controls; higher GCS (oral versus inhalational) the more the risk.

- All patients should be on multi-vitamins and CA – children and adults regardless of health status. Weight-bearing exercises important.

- Rx prophylactically when patient placed on systemic GCS for prolonged period or continuously. Probably indicated for those on prolonged very high doses of inhalational GCS – at least these patients should be monitored carefully.
Conclusions (cont’d)

- DXA important to screen and follow-up

- Responsibility of ALL physicians, regardless of specialty, to screen and Rx.

- Referral when case complicated or in doubt.
Recommendations for High Risk Subjects

- Follow low risk and moderate risk recommendations
- 24 hour urine for calcium and creatinine if receiving systemic CS therapy
- Bone densitometry
- Consider referral or detailed medical evaluation
Other Therapies of Osteoporosis

- Thiazide diuretics
- Hormone replacement therapy
- Bisphosphonates
- Calcitonin
- Selective estrogen receptor modulators
Bisphosphonate Options

- **Etidronate**
  - 200 mg bid, 2 weeks every 3 months

- **Alendronate**
  - 5 mg/day for at risk subjects
  - 10 mg/day or 70 mg/week for treatment

- **Risedronate**
  - 5 mg/day or 35-40 mg/week?
  - Reduced GI toxicity
Effect of Raloxifene on Incident Vertebral Fractures in Postmenopausal Women With Osteoporosis


* RR=0.5, 95% CI=0.3-0.7.  †RR=0.7, 95% CI=0.6-0.9.
††RR=0.6, 95% CI=0.4-0.9.  §§RR=0.5, 95% CI=0.4-0.6.
Intranasal Salmon Calcitonin: 5-Year Results of the PROOF Trial

% of patients with $\geq 1$ new fracture per year

- Placebo (n=270)
- 100 IU calcitonin (n=273)
- 200 IU calcitonin (n=287)
- 400 IU calcitonin (n=278)

*P <0.05 vs. placebo.

Long-Term Effect of Alendronate on BMD in Postmenopausal Women With Osteoporosis

Effect of Risedronate on Hip Fracture Risk in Women 70-79 Yrs. of Age With PMO

*RR=0.6, 95% CI=0.4-0.9.

Effect of Once-Weekly Alendronate in Postmenopausal Women With Osteoporosis


- 10 mg once daily (n=370)
- 35 mg twice weekly (n=369)
- 70 mg once weekly (n=519)

% change from baseline in BMD (12 mos.)*

*All changes were significant increases from baseline ($P < 0.05$).

Spine, Total hip, Femoral neck, Trochanter, Total body
Other Therapies of Osteoporosis

- Testosterone
- Pharmacologic dosages of Vitamin D
- Low dosages of PTH
- Growth hormone
- Fluoride
- 1,25 (OH)2 Vitamin D
Effect of PTH on Fracture Risk in Postmenopausal Women


- \*RR = 0.35, 95% CI = 0.22-0.55.
- †RR = 0.47, 95% CI = 0.25-0.88.
- ‡RR = 0.31, 95% CI = 0.19-0.50.
- §RR = 0.46, 95% CI = 0.25-0.86.
Potential Effects of Statins on Osteoporosis

- JAMA 2000;283:3211
- Bisphosphonates predominately affect bone resorption
- Statins predominately seem to increase bone formation
- Current statins may not be as effective
Needs for Optimal Assessment and Treatment of Osteoporosis

- Long term, large population data to determine if a threshold dosage of ICS exists
- Cost-effective screening or monitoring tests
- Treatments which enhance bone formation
- Increased awareness of osteoporosis in asthma
Needs for Optimal Assessment and Treatment of Osteoporosis

- Optimal utilization of asthma therapies which do not affect or have the potential to affect bone metabolism
- Additional studies of ICS during years when peak bone mass is achieved
- Better definition of fracture threshold
- Determination of value of treatment in subjects receiving “high dose” ICS
Cost of Osteoporosis Diagnosis and Treatment

- Patients already receiving expensive therapy
- Will adherence decrease with asthma therapy?
- Is assessment cost effective?

“...I see that you have a 20 percent deductible clause in your health insurance plan. That means we can only make you 80 percent well.”

NATIONAL ENQUIRER
"When the nurse said, 'Strip to the waist,' Mr. Hughes . . ."
Bone Densitometry

- Desk top low-dose X-ray using phosphor technology storage
  - $40/ test
  - Primarily cortical bone
- Ultrasound devices
  - Heel, calcaneous bone
  - Accuracy improving
## Relevance of BMD Changes to Fracture Risk Reduction

<table>
<thead>
<tr>
<th>Strengths</th>
<th>Weaknesses</th>
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<tbody>
<tr>
<td>• BMD measurement is the most accurate and precise means of assessing</td>
<td>• Impact of changes in BMD on fracture risk is not bidirectional</td>
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<tr>
<td>skeletal fragility</td>
<td>• Lack of uniformity exists among current BMD testing standards</td>
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<tr>
<td>• BMD is the strongest available predictor of initial fracture risk</td>
<td>• Many factors other than BMD also have an impact on fracture risk</td>
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<tr>
<td>• BMD increases correlate with fracture risk reduction</td>
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Problems with Studies of Osteoporosis

- Technology
- Time factor
- Disease effects independent of Rx effects
- Other previous, intermittent and/or concurrent Rxs
- Variable dosages of CS and ICS
- Various CS products
- At risk individuals vs mean data
Recommendations for Low Risk Subjects

- Maintain adequate calcium intake
- Encourage exercise, particularly weight bearing
- Consider Vitamin D supplementation
- Discourage cigarette smoking and significant EtOH
- Ensure euthyroid, consider measuring TSH
Daily Calcium Recommendations

- 800 mg/day for 1-10 years of age
- 1200 mg/day for 11-12 years of age
- 1200 mg/day for pregnancy and lactation
- 1000 mg/day for adults > 24 years of age
- 1500 mg/day for postmenopausal women
Vitamin D Recommendations

- Levels at upper limits of normal recommended for individuals at risk (400-800 units /day)
- Alfacalcidol 1 mcg/d ? recommended if higher risk (Arth Rheum 2001;44:1496)
- Pharmacologic dosages controversial
- 1,25 (OH)2 Vitamin D controversial
Recommendations for Moderate Risk Subjects

- Follow low risk recommendations
- Measure annual height
- Consider estrogen replacement or estrogen receptor modulator if peri/postmenopausal
- Consider bone densitometry
Effect of Low-Dose Estrogen Therapy on BMD in Postmenopausal Women

- 406 postmenopausal women were randomly assigned unopposed ERT (estrogen 0.3 mg/d, 0.625 mg/d, or 1.25 mg/d) or placebo
  - all ERT doses significantly increased lumbar spine BMD vs. baseline and placebo at 6, 12, 18, and 24 months
  - occurrence of endometrial hyperplasia was clinically relevant only at ERT doses of 0.625 mg/d and 1.25 mg/d
- 128 Caucasian women >65 yrs. with BMD of 0.90 g/cm² or less were randomized to low-dose HRT (estrogen 0.3 mg/d and medroxyprogesterone 2.5 mg/d) or placebo
  - spine BMD increased 3.23% vs. placebo (P <0.001)
  - HRT-related symptoms were mild and short-lived

Epidemiology of Osteoporosis

- Peak bone density (T score)
  - 30-35 years of age for cortical bone
  - < 30 years of age for trabecular bone
- Cortical bone loss ≈ 0.5-1%/year starting at ~ 40 years of age (Z score)
- Trabecular bone loss starts at ~ 35 years
  - 1-1.2% per year for men
  - 1-4.0% per year for women
  - 10% per year for 5-7 years perimenopausal
Other Therapies of Osteoporosis

- Testosterone
- Pharmacologic dosages of Vitamin D
- Low dosages of PTH
- Growth hormone
- Sodium Fluoride
- 1,25 (OH)2 Vitamin D
- Thiazide diuretics
Non-FDA-Approved Drugs for Osteoporosis

Calcitriol

- Synthetic vitamin D analogue, promotes calcium absorption
- Approved for managing hypocalcemia and metabolic bone disease in renal dialysis patients
- Also approved for hypoparathyroidism, both surgical and idiopathic, and pseudohypoparathyroidism
- No reliable data on efficacy
Other Bisphosphonates

Etidronate (200 mg BID, 2 weeks every 3 months), ibandronate, pamidronate, tiludronate, zoledronic acid

- Zoledronate – new bisphosphonate – perhaps used yearly
- In same class as other bisphosphonates
- None approved for prevention or treatment of osteoporosis
- Most medications approved for Paget’s disease, hypercalcemia of malignancy, and myositis ossificans
Sodium Fluoride

- Stimulates the formation of new bone
- The quality of bone uncertain
- Evidence that fluoride reduces fracture risk in conflicting and controversial
Effect of Low-Dose Estrogen Therapy on BMD in Postmenopausal Women

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Combination HR and Alendronate

• Combined therapy at femoral and vertebral sites > one or other

• Alendronate > HR > placebo

• Combined Rx may be option for severe disease or those that fail to respond

Mean (SEM) Percentage Change in Bone Mineral Density From Baseline for 36 Months HRT indicates hormone replacement therapy; ALN, alendronate.

Effects of Alendronate on Biochemical Markers of Bone Resorption in 259 Patients (Top Panel) and Bone Formation in 264 Patients (Bottom Panel) Receiving an Average Daily Dose of at Least 7.5 mg of Prednisone (or Its Equivalent). All values are means (+/- SE). The solid horizontal lines indicate the mean reference values for premenopausal women, and the dotted horizontal lines 1 SD above and below the mean. The values were significantly decreased at 48 weeks in the patients receiving 5 mg of alendronate and those receiving 10 mg (P<0.001).

**Alendronate Prevents and Treats GCS-Induced Osteoporosis**

- 48-week random, placebo-controlled study of alendronate 5 or 10 mg in 477 ♂ and ♀, 17-83 yoa, requiring at least one year oral GCS daily 7.5 mg or greater.

- Protects against ↓ bone density in lumbar-spine, hip and total bone density. Proportionally fewer new vertebral fractures in Rx group.

- Benefit not related to age, sex, underlying disease, dose of GCS. 5 or 10 mg similar results.

Effects of Alendronate on Bone Mineral Density in All Patients Receiving an Average Daily Dose of at Least 7.5 mg of Prednisone (or Its Equivalent)

Fall Prevention

- Check and correct vision
- Check hearing
- Evaluate for neurological problems
- Review medications for side effects that affect balance and stability
- Provide check list for home safety
- Wear undergarments with hip protectors (brands: Safehip®, HIPS®, HipGuard®, ImpactWear®)