

OSTEOPOROSIS

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Definitions

OSPS: Definition

“OSPS is a condition in which the bones have a propensity to fracture spontaneously or as a result of minimal trauma. In this condition...there is too little bone tissue to provide adequate skeletal support for the physical stresses of normal daily life...”

Barzel US "Osteoporosis" *Conn's Current Therapy*
Saunders (Philadelphia) 2007:714-718

Osteoporosis: WHO Guidelines

- Normal bone density = < 1 SD below mean
- Osteopenia = 1-2.5 SD below mean
- Osteoporosis = > 2.5 SD below mean
- Severe osteoporosis = > 2.5 SD below mean + fractures

Nattiv A. "Osteoporosis: Its prevention, recognition, and management" *Fam Pract Recert* 1998, 20 (2):17-41

Scope of the Problem

Women with OSPS: Their Perceptions (Gallup Survey, n= >1000)

Wish they had known known preventive measures	>50%
Believed OSPS unavoidable	>50%
Tried to prevent before Dx	33%
Discussed with MD pre-Dx	14%
Aware that meds Rx and prevent	±50%
Would have taken Rx, knowing what they know now	87%

Health and Medical Report *The Female Patient* 2000;25(August):17

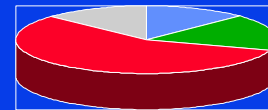
OSTEOPOROSIS (OSPS) Risk in Perspective

lifetime
risk hip Fx

>

breast CA
+
endometrial CA
+
ovarian CA

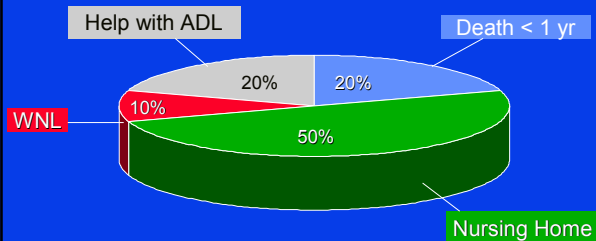
Nattiv A. "Osteoporosis: Its prevention, recognition, and management" *Fam Prac Recert* 1998; 20 (2):17-41



Death < 1 yr
NH Care
ADL Help
Home/Self Sufficient

Barzel US "Osteoporosis" *Conn's Current Therapy*
Saunders (Philadelphia) 2007:714-718

Hip Fx: Outcomes



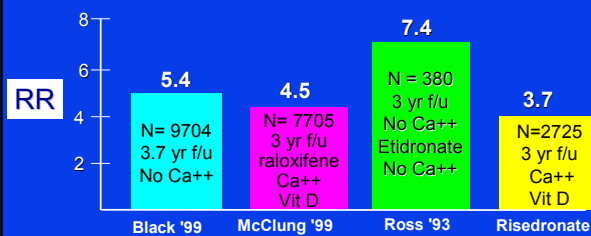
Barzel US "Osteoporosis" *Conn's Current Therapy*
Saunders (Philadelphia) 2007:714-718

OSPS : What's the Consequence?

- Lifetime risk of hip Fx for 50 year old Caucasian woman = 50%
- 50% post hip Fx survivors unable to walk unassisted
- 25% post hip Fx confined to long-term care facilities

Ettinger B "Maintaining Skeletal Health Among Postmenopausal Women" *Am J Managed Care* 1998;4:387-396

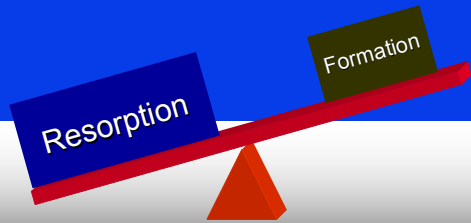
Vertebral Fx Begets Vertebral Fx



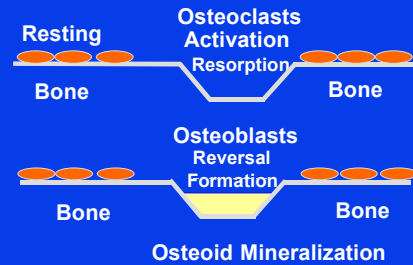
Black DM, et al. *J Bone Miner Res.* 1999;14(5):821-828.
McClung M, et al. *JAMA.* 1999;282(7):687-689. Ross PD, et al. *Osteoporosis Int.* 1993;3:120-126

Pathophysiology

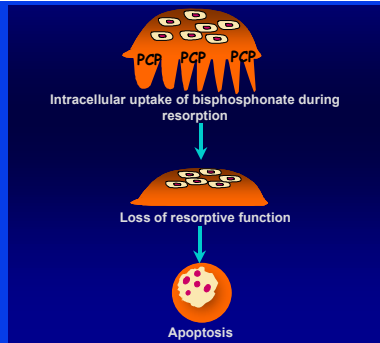
OSPS: MECHANISM



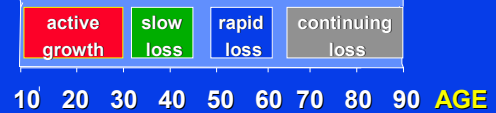
Bone Remodeling



Bisphosphonates and Osteoclasts



bone mass



Wasnich RD, et al *Osteoporosis. Critique and Practicum*. Honolulu, HI. Banyan Press, 1989

Post-Peak Bone Loss Patterns

Women

- 0.3%-0.5% yearly until menopause
- 1%-2% at menopause up to 5%

Men

- 0.2%-0.5% yearly

Nattiv A. "Osteoporosis: Its prevention, recognition, and management" *Fam Pract Recer* 1998; 20 (2):17-41

OSPS Risk Factors

OSPS RISK FACTORS

<u>Modifiable</u>	<u>Treatable</u>	<u>Unmodifiable</u>
Smoking	↓Estrogen	Gender
Sedentary	HyperT ₄	Menopause Age
XS ETOH	Cushing's	Race
Caffeine	Anorexia	Skeletal Habitus
Thyroid	Vit D ↓	Family Hx
Meds		
Steroids		
Dietary Ca ⁺⁺		

OSPS & Smoking

- Mechanism ?
- Supplementation Studies: smoking → ↓ Ca⁺⁺ absorption
- Twin studies : smoking 1 ppd → 5-10% BMD deficit by menopause

Lindsay R, Watts NB, Shoupe D. "Current Approaches to OSPS Prevention" *Am J Managed Care* 1998 ; 4 (2, Supp) : S64-S69

OSPS Dx

WHO Criteria: BMD

Diagnostic Criteria*	Classification
T= 0 to -1 SD	Normal
T= -1 to -2 SD	Osteopenia
T≤ -2.5 SD	Osteoporosis
T ≤ -2.5 SD + fragility fractures	Severe osteoporosis

BMD measurement: Which Tool?

"Although several methods exist, dual-energy x-ray absorptiometry (DEXA) is the most accurate method for assessing BMD in nearly all clinical settings"

Nattiv A. "Osteoporosis: Its prevention, recognition, and management" *Fam Prac Recert* 1998; 20 (2):17-41

Dx

"Measurement of BMD by DEXA is the current gold standard for the early recognition of osteoporosis in clinical practice."

Barzel US "Osteoporosis" *Conn's Current Therapy Saunders* (Philadelphia) 2007:714-718

OSTEONECROSIS



Johnson K "Watch for Osteonecrosis With Long-Term Bisphosphonates" *Fam Pract News* 2005(May1):58

DEXA: For Whom?

"...every woman who enters the menopause should undergo determination of her bone density"

Barzel US "Osteoporosis" *Conn's Current Therapy* Saunders (Philadelphia) 2007:714-718

DEXA: If WNL, When to Repeat?

- "If the density is normal, it can be rechecked 5-7 years later...."
- "If it is still normal, it is probably reasonable not to be concerned about bone density until the patient is 65 years old."

Barzel US "Osteoporosis" *Conn's Current Therapy* Saunders (Philadelphia) 2007:714-718

Dual-energy X-ray Absorptiometry (DEXA)

- Procedure of choice for BMD
- Used at wrist, spine, hip
- Radiation = 1.5 mRems (\cong 1/10 avg CXR)
- Cost \pm \$200 per procedure
- Device cost \pm \$70,000

Freeman R, "The Management of the Patient with OSPS" *Am J Manage Care* 1998; 4 (2,Sup): S94-S107

OSPS Dx: Minimum Lab

- Ca⁺⁺
- 25-OH Vitamin D
- PTH
- TSH
- 24-hr Urine: Ca⁺⁺ Na⁺, Creatinine
- N-Telopeptide (second morning urine)
- Osteocalcin

Barzel US "Osteoporosis" *Conn's Current Therapy* Saunders (Philadelphia) 2007:714-718

Bone Densitometry : Potentials

- Identify candidates for antiresorptive Rx
- Assist decision process for HRT
- Identify HPTH patients indicated for surgery (OSPS \rightarrow surgery)
- Reassessment of adequacy of Rx response
- Monitor medication effect on BMD
- f/u impact estrogen stressors (e.g., anorexia)

Freeman R, "The Management of the Patient with OSPS" *Am J Managed Care* 1998;4(2,Sup):S94-S107

BMD: INDICATIONS

- Hip Fx (any low-impact Fx)
- Anorexic (chronic or recurrent)
- Passive Immobilization (>2 weeks)
- Chronic Meds (seizure, T₄, steroids)
- FHx
- X-ray Osteopenia
- Smoker?


Nattiv A. "Osteoporosis: Its prevention, recognition, and management" *Fam Prac Recert* 1998; 20 (2):17-41

Who Should Get BMD Tested? WHO and NOF 2004

- All men and women > 65
- All women < 65 with risk factors
- Anyone with osteoporotic Fx
- Height loss > 2 cm
- Any vertebral compression Fx
- Glucocorticoid Therapy
- Hyperparathyroidism
- Women considering Rx
- All persons on Rx

Birge SJ "Osteoporosis" *Conn's Current Therapy* 2004
Rake and Bope, Eds Saunders (Philadelphia)

BMD as an ERT Motivator

- Study: 140 recently menopausal , undecided about ERT
- Rx: (A) Educational OSPS brochure + coupon for future BMD vs (B) OSPS brochure + immediate BMD
- Results(% pts ERT Rx): A = 20% B = 64%

Lindsay R, Watts NB, Shoupe D. "Current Approaches to OSPS Prevention" *Am J Managed Care* 1998; 4 (2, Sup): S64-S69

SHOULD BMD Be the Ultimate Arbiter? Dx Yes, Rx No

"BONE DENSITOMETRY CAN CLOUD THE CLINICAL PICTURE"

Kilgore C. "Bone Densitometry Can Cloud Clinical Picture" *Family Practice News* 2000; August 13:14

SHOULD BMD Be the Ultimate Arbiter? Dx Yes, Monitor Rx No

- Basic physician belief: \uparrow BMD = \downarrow Fx risk
- Fluoride \rightarrow \uparrow \uparrow BMD but no \downarrow Fx risk
- Ca⁺⁺, Vit D, SERMs, bisphosphonates \rightarrow \downarrow Fx risk with small \uparrow BMD
- 20-25% Fx risk reduction unrelated to BMD

Kilgore C. "Bone Densitometry Can Cloud Clinical Picture" *Family Practice News* 2000; August 13:14

If at first you don't succeed.....

- CONTEXT: Regression to the mean predicts pts with unusual Rx responses may later demonstrate 'typical' responses, if followed over time
- OBJECTIVE: See if women with \downarrow BMD on Rx during year 1 continue to lose in year 2 (same Rx)
- STUDY Rx: PMP on alendronate 5mg/d (n=2634) or raloxifene 60-120 mg/d (n=3954) X 2 years

Cummings SR, Palermo L, Browner W, et al "Monitoring OSPS Therapy with Bone Densitometry" *JAMA* 2000;283:1318-1321

If at first you don't succeed.....

"Most women who lose BMD during the first year of Rx... will gain BMD if the same Rx is continued for a second year... effective Rx for OSPS should not be changed because of loss of BMD during the first year of use"

Cummings SR, Palermo L, Browner W, et al "Monitoring OSPS Therapy with Bone Densitometry" *JAMA* 2000;283:1318-1321

Low BMD: Evaluation

"The single most important [biochemical] measure is 24-hour urinary excretion of calcium and creatinine on a known intake of calcium."

Birge SJ "Osteoporosis" *Conn's Current Therapy 2004*
Rake and Bope, Eds Saunders (Philadelphia)

The calcium-creatinine ratio 24-hour urine on 800-1200 mg/d Ca⁺⁺

- WNL = 0.15-0.25 mg
- > 0.25 = ↑ bone turnover/resorption
 - ♦ ↑PTH, ↑T4, renal Ca⁺⁺ loss, XS caffeine
- <0.15 = malabsorption, secondary PTH, vitamin D deficiency /resistance

Birge SJ "Osteoporosis" *Conn's Current Therapy 2004*
Rake and Bope, Eds Saunders (Philadelphia)

Vitamin D resistance

"Vitamin D resistance is an important diagnostic consideration in that it may affect up to 70% of patients with osteoporosis."

Birge SJ "Osteoporosis" *Conn's Current Therapy 2004*
Rake and Bope, Eds Saunders (Philadelphia)

Defining Vitamin D resistance

It can be operationally defined as a low 24-hr Ca⁺⁺:Cr ratio in the presence of normal serum 25-hydroxyvitamin D"

Birge SJ "Osteoporosis" *Conn's Current Therapy 2004*
Rake and Bope, Eds Saunders (Philadelphia)

OSPS : Basic Lab

- Ca⁺⁺
 - PO₄⁼
 - CBC
 - TSH
 - PTH
 - Vit D (25-OH)
- If clinical exam suggests:
- cortisol
 - ESR
 - Protein electrophoresis

Nattiv A. "Osteoporosis: Its prevention, recognition, and management" *Fam Prac Recert* 1998; 20 (2):17-41

Hyperparathyroidism

- ASx in >50% of affected
- Some postmenopausal OSPS trials → 10% pts ↑ PTH (Ca⁺⁺ WNL)
- PTH ↑ in Vit D deficiency

Freeman R, "The Management of the Patient with OSPS" *Am J Managed Care* 1998; 4(2,Sup):S94-S107

Bone Markers for Bone Turnover (BT)?

- ↑B T ⇔ ↑ bone loss rate
- ↑ BT pts → ↑ antiresorptive Rx response
- ↑ BT predicts ↑ Fx risk (independent of BMD in elder 📖)
- 3-6 months Rx should → ↓ urinary N-telopeptide or pyridinium cross-links

Nattiv A. "Osteoporosis: Its prevention, recognition, and management" *Fam Prac Recert* 1998; 20 (2):17-41

Bone Markers

- Used to monitor Rx efficacy
 - Do not identify ↓ BMD individuals
 - Cannot replace bone densitometry
- "Their cost effectiveness and correct use will have to await further study."

Freeman R, "The Management of the Patient with OSPS" *Am J Manage Care* 1998; 4(2,Sup):S94-S107

OSPS Prevention

Does HCTZ Actually Prevent OSPS?

- STUDY: Prospective cohort (n=7891)
- INCLUSION: Citizens of Rotterdam > 55
- METRIC: Hip Fx:HCTZ use/nonuse
- RESULTS: HCTZ > 1 year → HR 0.46
 - ◆ Not Dose Dependent
 - ◆ Benefits D-C after 4 month hiatus

Marlette WCJ, Schoofs et al *Ann Intern Med* 2003;139:476-482

OSPS Rx

Osteoporosis: Comparing Classes

	Prev	Rx	Spine Fx	Hip Fx
Estrogen	Yes	No	+++	+++
Alendronate	Yes	Yes	+++	+++
Risedronate				
Raloxifene	Yes	Yes	+++	+++
Calcitonin	No	Yes	+	+
PTH Hormone	No	Yes	++++	++++

Birge SJ "Osteoporosis" *Conn's Current Therapy* 2004
 Rake and Bope, Eds Saunders (Philadelphia)

Hips Fx Prevention: Hip Protectors

- STUDY: frail senior adults (n= 1409 women, 392 men, mean age 82)
- Rx: Hip protector padded undergarment
- MEASURED: Rx group Hip Fx when Fx number in control group = 62 (= 2 years)
- RESULTS: Relative hazard in hip protector group= 0.4 (includes non-compliant Fx)

Kannus P, Parkkari J, Niemi S, et al "Prevention of Hip Fx in Elderly People with Use of a Hip Protector" *N Engl J Med* 2000;343:1405-1513

Elemental Calcium

FORM	% Ca ⁺⁺	ELEMENTAL
Ca ⁺⁺ carbonate	40%	
Ca ⁺⁺ phosphate	30%	
Ca ⁺⁺ gluconate	9%	
Ca ⁺⁺ lactate	13%	

Example
 CaCO₃ tab = 600
 mg = 240 mg Ca⁺⁺

Hedlund LR, Gallagher, JC, "Estrogen Therapy for Postmenopausal Osteoporosis" *Ger Med Today* 1988; 7 (2) : 55-63

Clinical Question: "What is the Most Easily Absorbed Form of Calcium?"

- Ca⁺⁺ absorption dependent upon adequate Vit D, may ↓ with ↑age
- Food enhances absorption (± 20%↑)
- Phytic acid foods (spinach, rhubarb, wheat bran, unrefined flour) slow absorption
- absorption ↓ 20% at higher dose (1000 mg) vs lower (300 mg) → recommendation ≤500 mg/meal

Raisz LG. "Maximizing Calcium Absorption" *Consultant* 2000;September 15:1925

Clinical Question: "What is the Most Easily Absorbed Form of Calcium?"

"In sum, there is little evidence that the various Ca⁺⁺ salts differ in efficacy. Encourage pts to choose whatever form of Ca⁺⁺ supplementation they can best tolerate and comply with"

Raisz LG. "Maximizing Calcium Absorption" *Consultant* 2000;September 15:1925

**OSPS Rx:
 Estrogen**

Estrogen : OSPS equivalency

MINIMAL EFFECTIVE DAILY DOSES

Conjugated estrogen = 0.625 mg
Ethinyl estradiol = 20 mcg
Mestranol = 25 mg
Estradiol-17 β = 1 mg
Estrone sulfate = 1 mg
Transdermal = 50 mcg

Hedlund LR, Gallagher, JC, "Estrogen Therapy for Postmenopausal Osteoporosis" Ger Med Today 1988; 7 (2) : 55-63

OSPS Rx Bisphosphonates

OSPS Rx Vitamin D

Vitamin D RDA

Children	200 IU/d
18-50 yrs	200 IU/d
50-70 yrs	400 IU/d
>70 yrs	600 IU/d
PG/Lactation	600 IU/d



Ca⁺⁺ RDA

Children	500-800 mg/d
Teens	1300 mg/d
20-50 yrs	1000 mg/d
>50 yrs	1200 mg/d
PG/Lactation	100-1300 mg/d



Vitamin D : Repletion



- Drisdol
 - ♦ capsule 50,000 U 1-2 X weekly
 - ♦ Walgreen's Online: 30 @ \$65.95

<http://www.walgreens.com/library/finddrug/druginfo1>
accessed Sept 1-, 2007


Severe OSPS (T Score < - 4.0) Teriparatide

- Teriparatide (Forteo) 750 mcg/3mL
 - ◆ dose: 20 mcg SQ qd
 - ◆ Walgreen's Online: 3 mL @ \$795.99

<http://www.walgreens.com/library/finddrug/druginfo1>
accessed Sept 1-, 2007

Medication	Class	Mechanism	BMD Δ*	
Teriparatide	PTH	↑ formation	12%	
Alendronate	BisPhos	↓ resorption	±6%	
Risedronate	BisPhos	↓ resorption	±6%	
Ibandronate	BisPhos	↓ resorption		
Raloxifene	SERM	↓ resorption	3%	
Calcitonin				
Teriparatide + alendronate				↑ local FIRST YEAR change

Bisphosphonates

- Alendronate: 10 mg QD → ↑ BMD spine, hip, total body
 - ◆ → ↓ vertebral Fx, progression of vertebral deformity, height loss
 - ◆ → ↓ nonvertebral Fx at least 3 years
 - ◆ In  with vertebral Fx, → ↓ new Fx

Nattiv A. "Osteoporosis: Its prevention, recognition, and management" *Fam Prac Recer* 1998; 20 (2):17-41

Alendronate (Fosomax)

- Poor GI absorption : ± 0.75% PO dose
- Rapid effect: <24hrs, ≈70% bound to bone
- Bone t-1/2 = 10 years (administer daily to impact new resorption surfaces)
- effect of ↓ Creatinine Clearance ? (not recommended < 35 mL/min)

Kirk JK, Spangler JG. "Alendronate: A Bisphosphonate for Treatment of Osteoporosis" *Am Fam Phys* 1996; 54(6) : 2053-60

Alendronate (Fosomax)

- Side effects(<10%): nausea, abdominal pain, dyspepsia, diarrhea, vomiting, constipation
- Calcium in GI tract rapidly → ↓ absorption
- IV: Myalgias, arthralgias, fever, hypocalcemia

Kirk JK, Spangler JG. "Alendronate: A Bisphosphonate for Treatment of Osteoporosis" *Am Fam Phys* 1996; 54(6) : 2053-60

"Prevention of Nonvertebral Fractures by Alendronate"

- Meta-analysis 5 studies (n=1,602)
- All pts 42-85 years old, T-score < -2.0
- Rx group vs placebo group RR = 0.71
- Conclusion: "Rx with alendronate ↓ risk of nonvertebral Fx over at least 3 years."

Karpf D , Shapiro R, Seeman E, et al. *JAMA*.1997;277:1159-1164

Alendronate : How Effective?

- Study: postmenopausal OSPA (n = 994)
- Rx: alendronate PO 5-10mg/d X 3 years, or 20 mg/d X 2 years then 5 mg/d X 1 year
- Results
 - ◆ ↑ BMD: spine 8.8%, femur 5.9-7.8%
 - ◆ ↓ Fx: vertebral 46%, stature loss 35%

Kirk JK, Spangler JG. "Alendronate: A Bisphosphonate for Treatment of Osteoporosis" *Am Fam Phys* 1996; 54(6) : 2053-60

Alendronate : Administration

- any food or non-water liquid can → ↓ absorption (±60%)
- even high Ca⁺⁺ water can → ↓ absorption
- administer with 8oz water 30 mins before any other PO intake
- non-recumbency for > 30 minutes postdose
- cost (AWP) ± \$41/month

Kirk JK, Spangler JG. "Alendronate: A Bisphosphonate for Treatment of Osteoporosis" *Am Fam Phys* 1996; 54(6) : 2053-60

Alendronate + Estrogen?

- Animal studies +
- Limited data suggests no adverse effects, but bone benefits may not be additive
- alendronate vs calcitonin-NS : ↑ lumbar and femoral BMD only by alendronate

Kirk JK, Spangler JG. "Alendronate: A Bisphosphonate for Treatment of Osteoporosis" *Am Fam Phys* 1996; 54(6):2053-60

Glucocorticoid-Induced OSPA

"Physicians should be aware that even low doses of corticosteroids can have important long-term effects on bone mass, and therefore, implementing preventive measures is necessary"

Buckley L. "Preventing corticosteroid-induced osteoporosis" *Hospital Medicine* 1997 (July):15-23

Glucocorticoid-Induced OSPA

- Osteocalcin ↓ < 1 week OCS Rx, stays ↓
- Most bone loss occurs early
- As little as 5 mg/d prednisone may ↓ BMD
- QOD Rx does not ↓ bone loss

Buckley L. "Preventing corticosteroid-induced osteoporosis" *Hospital Medicine* 1997 (July):15-23

Glucocorticoid-induced OSPA : Risedronate

- STUDY: RA and COPD MEN (n=186) on OCS; mean age = 58
- Rx: Risedronate 2.5-5 mg/d X 12 months
- Results: ↑BMD or reduction of BMD loss at LS Spine, Femur

Maricic M, Weryha G, Emkey R, et al "Risedronate Increases Bone Mass in Men Receiving Glucocorticoid Therapy" *Arthritis & Rheumatism* 2000;43(Suppl9)

Risedronate or Alendronate?

- STUDY: Healthy PMP women (n=515)
- Rx: alendronate 10 mg vs risedronate 5 mg qd
- MEASURED: Endoscopy at days 8 and 15
- RESULTS: Gastric ulcers risedronate = 4.1%, alendronate = 13.2%

Lanza FL, Hunt RH, Thomson ABR, et al "Endoscopic Comparison of Esophageal and Gastrointestinal Effects of Risedronate and Alendronate in Postmenopausal Women" *Gastroenterology* 2000;119:631-638

OSPS Rx SERMS

Selective Estrogen Receptor Modulators (SERM's)

- = estrogen agonism in some targets (e.g., bone) + neutrality or estrogen antagonism in other targets (breast, uterus)
- tamoxifen = 1st SERM
 - ◆ breast : estrogen antagonist
 - ◆ bone : estrogen agonist
 - ◆ uterus : estrogen agonist

McClung MR, Goldstein SR "Potential Impact of Emerging Rx's on OSPS Prevention" *Am J Manage Care* 1998; 4(2, Sup): S78-S84

Raloxifene : 2nd Generation SERM

- bone : estrogen agonist
- lipids : estrogen agonist
- breast : estrogen antagonist (antiproliferative to breast CA cells)
- uterus : neutral
- hot flashes frequency = tamoxifen

McClung MR, Goldstein SR "Potential Impact of Emerging Rx's on OSPS Prevention" *Am J Manage Care* 1998; 4(2, Sup): S78-S84

Raloxifene : Uterine Effects

- Study: 136 PMP no endometrial hyperplasia
- Rx: Raloxifene 10 mg/d vs cont combined HRT
- RESULTS: Endometrial Thickness (1 year):
 - HRT: 0.62mm (p<0.05)
 - Raloxifene: 0.18 mm (NS)

McClung MR, Goldstein SR "Potential Impact of Emerging Rx's on OSPS Prevention" *Am J Manage Care* 1998; 4(2, Sup): S78-S84

Raloxifene vs ERT: Uterine Effects

<u>Parameter</u>	<u>Raloxifene</u>	<u>HRT</u>
Endometrial Hyperplasia	0%	0%
Proliferative Endometrium	0%	31.6%
Uterine Polyp	0%	2.6%
Vaginal Bleeding → D-C	0%	8.7%

McClung MR, Goldstein SR "Potential Impact of Emerging Rx's on OSPS Prevention" *Am J Manage Care* 1998; 4(2, Sup): S78-S84



Raloxifene : European Prevention Study

- Study: 601 PMP women, age 45-60
- Rx: raloxifene (60 mg/d) vs placebo
- Results: Rx →
 - ♦ ↓ bone turnover (↓ urinary C-telopeptide)
 - ♦ ↑ BMD spine (2.4%), hip (2.4%)
 - ♦ ↓ LDL, no Δ HDL or TG
 - ♦ D-C rate = placebo

McClung MR, Goldstein SR "Potential Impact of Emerging Rxs on OSPS Prevention" *Am J Manage Care* 1998; 4(2, Sup): S78-S84

OSPS Rx Calcitonin

Calcitonin

- produced in thyroid parafollicular cells
- four species synthesized : pigs, salmon, rat, human
- All Calcitonin synthesized = 32 amino acids, #1-9 = same sequence all species
- efficacy in  = 




Aloia JF, "Calcitonin and Osteoporosis" *Ger Med Today* 1985;4:11

Calcitonin

- IM (approved 1984)
 - ♦ 50 IU 3X/wk for OSPS
 - ♦ 100 IU 5X/wk for painful OSPS
- NS (approved 1995)
 - ♦ one spray 200 IU QD
 - ♦ Can → nasal ulceration (uncommon)

Nattiv A. "Osteoporosis: Its prevention, recognition, and management" *Fam Prac Recer* 1998; 20 (2):17-41

Calcitonin in Menopause

- level  < 
- decline with age (?)
- lower levels in osteoporotic  (?)
- most effective in high bone turnover states
- side effects (IM) : flushing/warmth/ redness in face, palms, soles X 1 hour/ GI, urinary frequency → discontinuation <5%

Aloia JF, "Calcitonin and Osteoporosis" *Ger Med Today* 1985;4:11

Calcitonin : Actions

- Anti-hypercalcemic
 - ♦ ↓ bone resorption
 - ♦ ↑ urinary calcium excretion
 - ♦ ↓ intestinal calcium absorption
- ↓ osteoclast activity
- Blocks PTH-induced bone resorption

Aloia JF, "Calcitonin and Osteoporosis" *Ger Med Today* 1985;4:11

Calcitonin : Menopausal OSPS

- **STUDY:** x-ray osteoporosis + vertebral fx
- **Rx:** Calcitonin 50 IU sq QOD + adequate dietary calcium (500-1000 mg/d) [n=79]
- **RESULTS:**
 - (high turnover) \uparrow 22% spine bone mineral content, no Δ femur
 - (normal turnover) no Δ spine, ? benefit femur

Civitelli R, Bonnell S, Zacchei F, et al. "Bone Turnover in Postmenopausal osteoporosis" *J Clin Invest* 1988 ; 82 : 1268-1274

Vitamin D

- BMD \downarrow may represent osteomalacia (Vit D deficiency) not osteoporosis
- \pm 3% \downarrow BMD = Vit D deficiency
- Dx : serum Vit D level ; Rx : Vit D
- Renal dysfunction \rightarrow \downarrow conversion dietary Vit D \rightarrow 1, 25 dihydroxycholecalciferol
 - Dx : serum 1, 25 dihydroxycholecalciferol
 - Rx : Calcitriol

Freeman R, "The Management of the Patient with OSPS" *Am J Manage Care* 1998 ; 4 (2,Sup): S94-S107

Vitamin D Rx

- Usual dose = 400 IU
- Vit D resistance may require up to 10-20,000 u/day
 - Drisdol 50,000 u/capsule Q1month
- Monitor adequacy by I creasing dose Q3months until $Ca^{++}:Cr = 0.15-0.20$

Birge SJ "Osteoporosis" *Conn's Current Therapy* 2004
Rake and Bope, Eds Saunders (Philadelphia)

OSPS : Exercise

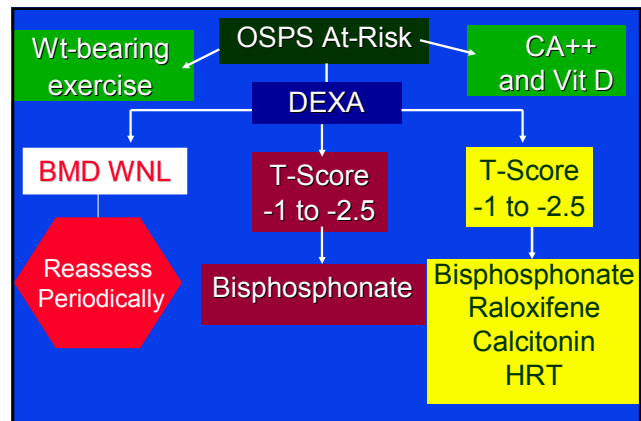
- Must be weight bearing
- \rightarrow \uparrow BMD & \downarrow incidence falls

Lindsay R, Watts NB, Shoupe D. "Current Approaches to OSPS Prevention" *Am J Managed Care* 1998 ; 4 (2, Sup) : S64-S69

OSPS Prevention : Exercise

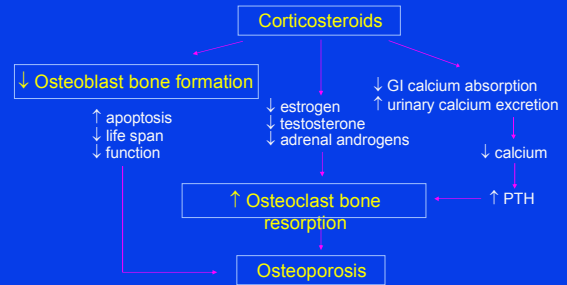
- Xsect studies: regular wt. bearing exercise \rightarrow BMD $>$ sedentary
- BMD \uparrow (site specific) with loading
- exercise \rightarrow slight \uparrow BMD in sedentary
- 30 minutes walking daily \rightarrow \downarrow risk vertebral hgt loss

Nattiv A. "Osteoporosis: Its prevention, recognition, and management" *Fam Prac Recert* 1998; 20 (2):17-41



Oddz & Ends

Pathophysiology of CIO: Bone Formation and Resorption



↑ Fx and Carbonated Beverages

- **STUDY:** X-sect retrospective study (n=409) 10th grade girls
- **MEASURED:** carbonated beverage association with bone fracture
- **RESULTS:** Carbonated Drink Intake Fx Odds Ratio = 3.14, Cola = 4.94

Wyshak G. "Teenaged Girls, Carbonated Beverage Consumption, and Bone Fractures" *Arch Ped Adolesc Med* 2000;143:610-613

COPD → ↑OSPS

- **STUDY:** X-sect survey COPD pts (n=171) age 23-90
- **MEASURED:** BMD, steroid Rx (PO or MDI)
- **RESULTS:** COPD → ↑RR 5X OSPS (> in steroid users)

Iqbal F, Michaelson J, Thaler L, et al "Declining bone mass in men with COPD" *Chest* 1999;116:1616-1624

COPD → ↑OSPS

Pulmonary Reviews 2000 (Feb):1-15

"All of the men with COPD had lost bone mass, regardless of whether they were taking corticosteroids-which indicates that COPD is an independent risk factor for OSPS"

Iqbal F, Michaelson J, Thaler L, et al "Declining bone mass in men with COPD" *Chest* 1999;116:1616-1624

OSPS Rx in Men

- **STUDY:** Osteoporotic men (n=241)
 - **Rx:** alendronate 10 mg, Ca⁺⁺, Vit D X 2 years
- | BMD OUTCOME: | alendronate | Placebo |
|------------------|-------------|---------|
| • LS spine | ↑7.1% | ↑1.8% |
| • Femoral neck | ↑2.5% | ↓ |
| • Hip Trochanter | ↑4.4% | ↑1.3% |
- VERTEBRAL Fx OUTCOME: 0.8% vs 7.1%

Orwoll E, Ettinger M, Weiss S, et al. "Alendronate for the Treatment of Osteoporosis in Men" *N Engl J Med* 2000; 343:604-10

OSPS & Low Dose HCTZ

- **STUDY:** RDBPC (n=3250) healthy normotensive pts
- **Rx:** HCTZ 12.5 or 25 mg/d vs placebo X 36 months
- **MEASURED:** BMD hip, LS spine, total body
- **RESULTS:** Small ↑BMD (.5-1%) at 6 months, declines over time

LaCroix AZ, Ott SM, Ichikawa L, et al. "Low-dose HCTZ and preservation of BMD in older adults" *Ann Intern Med* 2000;133:516-26

Vitamin A and OSPS

- **PREMISES:**
 - ♦ 1) Highest OSPS Fx rate in northern Europe, with unusually high dietary Vitamin A intake
 - ♦ 2) Animal studies: most common adverse Vitamin A toxic dose effect = spontaneous Fx
- **STUDY:** Xsect study (n=422) adult women with hip Fx compared to controls
- **RESULTS:** for every 1 mg/d ↑intake retinol, hip fracture risk ↑68%

Melhus H, Michaelsson K, Kindmark a, et al. "Excessive Dietary Intake of Vitamin A Is Associated with ↓ BMD and ↑ Risk for Hip Fracture" *Ann Intern Med* 1998;129:770-778

Diuretics: Osteoporosis

