Thyroid Nodules, Vitamin D and Osteoporosis

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Disclosures

• None
Objectives

1. Evaluation of thyroid nodules

2. Management of thyroid nodules based on the results of fine needle aspiration

3. Role of Vitamin D in human health

4. Evaluation of patients with low bone mineral density

5. Treatment options for patients with low bone mineral density and osteoporosis
Thyroid Nodules
Definition

- A thyroid nodule is a distinct lesion within the thyroid gland which radiologically distinct from the surrounding thyroid parenchyma.
How Common Are Thyroid Nodules?

![Graph showing the prevalence of thyroid nodules with age, comparing USG and palpation methods.](image)

Mazzaferri NEJM 1993;328:553
First Step...Measure TSH

- Subnormal
  - Radioactive iodine uptake and scan

Stocker et.al. Thyroid. 2002

Soule et.al. Thyroid. 2001
If TSH is Normal or Elevated…

• Perform thyroid USG
What is the role of Fine Needle Aspiration (FNA) biopsy?

• Accurate and cost effective

• Procedure of choice in evaluation of thyroid nodules

• USG guidance recommended for nodules that are non palpable, posteriorly located or predominantly cystic
Which nodules should be evaluated by FNA?

• Generally, only nodules > 1 cm

• < 1 cm with “suspicious” USG findings:
  – Associated lymphadenopathy
  – H/o thyroid cancer or thyroid cancer syndromes in first degree relative
  – Head/neck radiation

• $^{18}$FDG-PET positive
US Characteristics Predictive of Benign Nodule

- Hyperechoic nodule
- Spongiform nodule

Yoon et al. J Ultrasound Medicine. 2007
US Characteristics Suspicious for Malignancy

Smith-Bindman et.al. JAMA 2013;173:1788
US Characteristics Suspicious For Malignancy

Dai et. al. Thyroid 2010; 20:51
## Cytopathological Interpretation of Thyroid Nodules

Bethesda system of reporting thyroid Cytopathology

Implied risk of malignancy and recommended clinical management

<table>
<thead>
<tr>
<th>Diagnostic Category</th>
<th>Risk of Malignancy (%)</th>
<th>Usual Management‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nondiagnostic or Unsatisfactory</td>
<td>1-4</td>
<td>Repeat FNA with ultrasound guidance</td>
</tr>
<tr>
<td>Benign</td>
<td>0-3</td>
<td>Clinical follow-up</td>
</tr>
<tr>
<td>Atypia of Undetermined Significance or Follicular Lesion of Undetermined Significance</td>
<td>~5-15‡</td>
<td>Repeat FNA</td>
</tr>
<tr>
<td>Follicular Neoplasm or Suspicious for a Follicular Neoplasm</td>
<td>15-30</td>
<td>Surgical lobectomy</td>
</tr>
<tr>
<td>Suspicious for Malignancy</td>
<td>60-75</td>
<td>Near-total thyroidectomy or surgical lobectomy§</td>
</tr>
<tr>
<td>Malignant</td>
<td>97-99</td>
<td>Near-total thyroidectomy§</td>
</tr>
</tbody>
</table>

Chibas and Ali Thyroid 2009;19:1159
Management of Multiple Thyroid Nodules

• In the presence of two or more thyroid nodules >1 cm, those with a suspicious sonographic appearance should be aspirated preferentially (B)

• If none of the nodules has a suspicious sonographic appearance and multiple sonographically similar coalescent nodules with no intervening normal parenchyma are present, the likelihood of malignancy is low and it is reasonable to aspirate the largest nodules only and observe the others with serial US examinations. (C)

American Thyroid Association Guidelines 2009
Long Term Follow Up of Thyroid Nodules

• Follow up all benign nodules with serial USG
  – 6-18 months after initial FNA

  If stable in size, increase follow up interval
  If evidence of growth, repeat FNA, preferably with US guidance

• There is ~ 5% false negative rate of FNA diagnosed benign thyroid nodules
  – Higher rate for nodules > 4 cm

American Thyroid Association Guidelines 2009
**Caveat in Management of Indeterminate Nodules**

- 15 - 30% of aspirates may be indeterminate
- Next step → surgery
- 2/3rd are benign - confirmed post surgery
- There is a 2 - 10% chance of post-op complications and most need lifelong Lt4 Rx
- 60-70% of thyroid cancers harbor at least one known genetic mutation
- Molecular analysis (BRAF, RAS, RET/PTC, PAX8-PPARY) are specific, but not sensitive
Advances in Management Of Indeterminate Nodules

• New gene-expression classifier test
• Used to identify low-risk thyroid nodules among cytologically indeterminate fine-needle aspirates
Management of Thyroid Nodules In Pregnant Women

• Measure TSH

• If suppressed (& persists after first trimester) wait until after pregnancy and lactation to perform RAI scan

• If normal / elevated, perform FNA
  – If nodule discovered early in pregnancy and + PTC
    – Repeat USG and surgery may be performed before 24 wks of gestation - if substantial growth is seen
  – If nodule is stable by mid-gestation OR Discovered late gestation
    – Delay surgery after delivery and consider Lt4 therapy - TSH goal 0.1-1

American Thyroid Association Guidelines 2009
Management of Thyroid Nodules In Children

• Diagnostic and therapeutic approach to one or more thyroid nodules in a child

• Should be the same as it would be in an adult

• Clinical evaluation, serum TSH, US, FNA (A)

American Thyroid Association Guidelines 2009
Role of Vitamin D in Human Health
Vitamin D is …

• Fat soluble vitamin from steroid family

• Main actions
  – Facilitates calcium absorption in intestinal tract
  – Helps maintaining serum calcium and phosphorus
  – Allows adequate mineralization of skeleton
  – Prevents
    – Rickets in children
    – Osteomalacia in adults
    – Osteoporosis in elderly
  – Affects muscle composition and strength
Vitamin D Nonskeletal benefits

- May regulate skin barrier and hair
- May play a role in cancer biology
- May lower cardiovascular disease
- May control the innate and adaptive immune responses in humans
- May influence maternal-fetal health
Vitamin D

The body makes vitamin D when it is exposed to Ultraviolet (UV) rays from the sun.

**FOOD SOURCES:**

Cheese  
Margarine  
Butter  
Fortified Milk  
Healthy Cereals  
Fatty Fish

dermaharmony.com

evitamins.com

Searchhomeremedry.com
Pathways of Vitamin D synthesis

7-dehydrocholesterol

UV light skin

Cholecalciferol (vitamin D3)

Liver

Calcidiol (25-hydroxyvitamin D)

Kidney

Calcitriol (1,25-dihydroxyvitamin D)

↑ Intestinal absorption of calcium

 ↑ Bone resorption

↓ Renal Ca++ and phosphate excretion

Diet/supplements

Ergocalciferol (vitamin D2)

Inactive metabolite (24,25-dihydroxyvitamin D)
Clinical Manifestations of Vitamin D Deficiency

Rickets

Osteomalacia

Looser fracture tibia
## Lab Findings

<table>
<thead>
<tr>
<th></th>
<th>Vitamin D Deficiency</th>
<th>Osteoporosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium</td>
<td>↓ or N</td>
<td>N</td>
</tr>
<tr>
<td>Phosphorus</td>
<td>↓ or N</td>
<td>N</td>
</tr>
<tr>
<td>ALP</td>
<td>↑</td>
<td>N</td>
</tr>
<tr>
<td>PTH</td>
<td>↑</td>
<td>N</td>
</tr>
<tr>
<td>24 (OH) Vit D</td>
<td>↓ ↓</td>
<td>↓ or N</td>
</tr>
<tr>
<td>1,25 di(OH) D</td>
<td>N or ↑ or ↓</td>
<td>N</td>
</tr>
</tbody>
</table>
Fracture Prevention with Vit D Supplementation

Bischoff-Ferrari JAMA 2005;293:2257
What is Sufficient Vitamin D Intake?

<table>
<thead>
<tr>
<th>Age</th>
<th>General Population (Institute of Medicine Recommendations)</th>
<th>At Risk of Vitamin D Deficiency (The Endocrine Society Suggestions)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RDA (IU/day)</td>
<td>Upper Limit (IU/day)</td>
</tr>
<tr>
<td>Infants and children</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–6 months</td>
<td>—</td>
<td>1,000</td>
</tr>
<tr>
<td>6–12 months</td>
<td>—</td>
<td>1,500</td>
</tr>
<tr>
<td>1–3 years</td>
<td>600</td>
<td>2,500</td>
</tr>
<tr>
<td>4–8 years</td>
<td>600</td>
<td>3,000</td>
</tr>
<tr>
<td>9–18 years</td>
<td>600</td>
<td>4,000</td>
</tr>
<tr>
<td>Adults</td>
<td></td>
<td></td>
</tr>
<tr>
<td>19–70 years</td>
<td>600</td>
<td>4,000</td>
</tr>
<tr>
<td>&gt;70 years</td>
<td>800</td>
<td>4,000</td>
</tr>
<tr>
<td>Pregnant or breast-feeding</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14–18 years</td>
<td>600</td>
<td>4,000</td>
</tr>
<tr>
<td>19–50 years</td>
<td>600</td>
<td>4,000</td>
</tr>
</tbody>
</table>

IU = International Units
Taking Vitamin D With the Largest Meal Improves Absorption and Results in Higher Serum Levels of 25-Hydroxyvitamin D

**Fig. 1.** Change in serum 25(OH)D levels before and after diet intervention observed in all patients.
Low Bone Mass, Osteoporosis and Fracture Risk Assessment
Burden - Low Bone Mass

• Based on NHANES III data

• NOF estimates that 33.6 million Americans have low bone density at hip

NOF- 2002
Burden - Osteoporosis

• By 2012, approximately 12 million Americans older than 50 years are expected to have osteoporosis

• **One half of all postmenopausal women will have an osteoporosis-related fracture** during their lifetime; 25% of these women will develop a vertebral deformity, and 15% will experience a hip fracture

• Osteoporotic fractures, particularly hip fractures, are associated with chronic pain and disability, loss of independence, decreased quality of life and increased mortality

• Although hip fractures are less common in men than in women, **more than one third of men who experience a hip fracture die within 1 year**
Osteoporosis (OP): Definition

• Silent skeletal condition characterized by *low bone mass* and *compromised bone strength* predisposing to an increased risk of fracture
Fragility Fracture

• Any fracture in adults (except for face and digits) that occurs from fall from a standing height and without major trauma
FIGURE 1. Micrographs of Normal vs. Osteoporotic Bone

Normal bone

Osteoporotic bone

From: Dempster, DW et al.\textsuperscript{6}, with permission of the American Society for Bone and Mineral Research.
WHO Relies on BMD to Define Osteoporosis

![Graph showing BMD (Bone Mineral Density) for Spine: L1-L4](ISCDBoneDensitometryClinicianCourseLecture5_2008)

T = -2.0  Z = -0.5

From: ISCD Bone Densitometry Clinician Course, Lecture 5 (2008)
**TABLE 4: Defining Osteoporosis by BMD**

The World Health Organization has established the following definitions based on BMD measurement at the spine, hip or forearm by DXA devices:\(^{13}\)

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Normal:</strong></td>
<td>BMD is within 1 SD of a “young normal” adult (T-score at -1.0 and above).</td>
</tr>
<tr>
<td><strong>Low bone mass (“osteopenia”):</strong></td>
<td>BMD is between 1.0 and 2.5 SD below that of a “young normal” adult (T-score between -1.0 and -2.5).</td>
</tr>
<tr>
<td><strong>Osteoporosis:</strong></td>
<td>BMD is 2.5 SD or more below that of a “young normal” adult (T-score at or below -2.5). Patients in this group who have already experienced one or more fractures are deemed to have severe or “established” osteoporosis.</td>
</tr>
</tbody>
</table>

**Note:** Although these definitions are necessary to establish the presence of osteoporosis, they should not be used as the sole determinant of treatment decisions.
Take Home Message

• Individuals with an osteoporotic fracture including a morphometric vertebral fracture have ‘clinical osteoporosis’ independent of their BMD
Take Home Message

• Bone mineral density was originally developed to diagnose a high risk for fragility fractures in older, postmenopausal women who may have primary osteoporosis

• However, use of BMD in a young healthy premenopausal women can lead to unexpected findings of low BMD
Practitioners should not assume that all women with a low T-score have osteoporosis.
BMD Contributes Partly To Skeletal Strength

- Diseases and drugs that increase BMD and increase risk of fragility fractures
  - Osteopetrosis
  - Fluoride

**Figure 2.** Estimated incidence of fracture as a function of age and bone mass in 521 white women followed for an average of 6.5 years.
Bone Quality

• Refers to structural and material composition of the bone that determine its strength

• Some contributing factors:
  – Micro architecture
  – Accumulated microscopic damage
  – Quality of collagen
  – Size of the mineral crystals
  – Rate of bone turn-over
FRAX
WHO Fracture Risk Assessment Tool

http://www.shef.ac.uk/FRAX/
Welcome to FRAX®

The FRAX® tool has been developed by WHO to evaluate fracture risk of patients. It is based on individual patient models that integrate the risks associated with clinical risk factors as well as bone mineral density (BMD) at the femoral neck.

The FRAX® models have been developed from studying population-based cohorts from Europe, North America, Asia and Australia. In their most sophisticated form, the FRAX® tool is computer-driven and is available on this site. Several simplified paper versions, based on the number of risk factors are also available, and can be downloaded for office use.

The FRAX® algorithms give the 10-year probability of fracture. The output is a 10-year probability of hip fracture and the 10-year probability of a major osteoporotic fracture (clinical spine, forearm, hip or shoulder fracture).

Dr. John A. Kanis
Professor Emeritus,
University of Sheffield

FRAX Desktop Application

Click here to view the applications available.

Web Version 3.7

View Release Notes

Links

www.iofbonehealth.org

www.nof.org

www.jpof.or.jp

www.esceo.org

FRAX available as iPhone App

View in iTunes

3875736

Individuals with fracture risk assessed since 1st June 2011
Welcome to FRAX®

The FRAX® tool has been developed for use in individual patient models and population-based cohorts from Europe, North America, Asia and Australia. It is available on this site in several simplified paper versions, based on the number of risk factors. The FRAX® tool is computer-driven and can be downloaded for office use. Several simplified paper versions are also available, and can be downloaded for office use.

The FRAX® algorithms give the 10-year probability of fracture. The output is a 10-year probability of hip fracture and the 10-year probability of a major osteoporotic fracture (clinical spine, forearm, hip or shoulder fracture).
Calculation Tool

Please answer the questions below to calculate the ten year probability of fracture with BMD.

**Questionnaire:**

1. Age (between 40-90 years) or Date of birth
   - Age: 65
   - Data of birth: Y: [ ], M: [ ], D: [ ]

2. Sex
   - Male
   - Female

3. Weight (kg)
   - 70

4. Height (cm)
   - 165.1

5. Previous fracture
   - No
   - Yes

6. Parent fractured hip
   - No
   - Yes

7. Current smoking
   - No
   - Yes

8. Glucocorticoids
   - No
   - Yes

9. Rheumatoid arthritis
   - No
   - Yes

10. Secondary osteoporosis
    - No
    - Yes

11. Alcohol 15 or more units per day
    - No
    - Yes

12. Femoral neck BMD (g/cm²)

Select DXA

Calculate

BMI: 25.7

The ten year probability of fracture (%)

without BMD
- Major osteoporotic: 9.1
- Hip fracture: 1.2

**Having trouble with the FRAX tool?**

If you experience any problems with the FRAX tool please upgrade your version of Adobe Flash. Click here to upgrade.

**For USA use only**
Calculation Tool

Please answer the questions below to calculate the ten year probability of fracture with BMD.

Country: US (Caucasian)  Name/ID:

Age: 65 Y  Date of birth: M: _______ D: _______

Gender: Male Female

Weight (kg): 70

Height (cm): 165.1

Previous fracture: No Yes

Parent fractured hip: No Yes

Current smoking: No Yes

Glucocorticoids: No Yes

Rheumatoid arthritis: No Yes

Secondary osteoporosis: No Yes

Alcohol 13 or more units per day: No Yes

Femoral neck BMD (g/cm²): T-score: -0.3

GE-Lunar h

BMI: 70.0

The ten year probability of fracture (%)

with BMD

- Major osteoporotic: 4.8
- Hip fracture: 0.1

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Calculation Tool

Please answer the questions below to calculate the ten year probability of fracture with BMD.

Country: US (Caucasian)  Name/ID:  

**Questionnaire:**

1. Age (between 40-90 years) or Date of birth
   - Age: 65
   - Date of birth:  
   - M:  
   - D:  

2. Sex  
   - Male
   - Female  

3. Weight (kg)  
   - 65

4. Height (cm)  
   - 165.1

5. Previous fracture  
   - No
   - Yes  

6. Parent fractured hip  
   - No
   - Yes  

7. Current smoking  
   - No
   - Yes

8. Glucocorticoids  
   - No
   - Yes

9. Rheumatoid arthritis  
   - No
   - Yes

10. Secondary osteoporosis  
    - No
    - Yes

11. Alcohol  
    - 13 or more units per day  
    - No
    - Yes

12. Femoral neck BMD (g/cm²)  
    - Select DXA
    -  

**BMI:** 23.8

The ten year probability of fracture (%)

**BMI without BMD**

- Major osteoporotic: 18
- Hip fracture: 1.8

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**For USA use only**

01340444

Individuals with fracture risk assessed since 1st June 2011

DOS CME Course 2014
Calculation Tool

Please answer the questions below to calculate the ten year probability of fracture with BMD.

Questionnaire:

1. Age (between 40-80 years) or Date of birth
   - Age: [65]
   - Data of birth: [Y: [ ], M: [ ], D: [ ]]  

2. Sex
   - Male
   - Female

3. Weight (kg)
   - [65]

4. Height (cm)
   - [165.1]

5. Previous fracture
   - No
   - Yes

6. Parent fractured hip
   - No
   - Yes

7. Current smoking
   - No
   - Yes

8. Glucocorticoids
   - No
   - Yes

9. Rheumatoid arthritis
   - No
   - Yes

10. Secondary osteoporosis
    - No
    - Yes

11. Alcohol 13 or more units per day
    - No
    - Yes

12. Femoral neck BMD (g/cm²)

Select DXA

Calculate

BMI 23.8

The ten year probability of fracture (%)

without BMD

- Major osteoporotic: 18
- Hip fracture: 1.8

BMI

Having trouble with the FRAX tool?

If you experience any problems with the FRAX tool please upgrade your version of Adobe Flash. Click here to upgrade.

For USA use only

DOS CME Course 2014
Calculation Tool

Please answer the questions below to calculate the ten year probability of fracture with BMD.

Country: US (Caucasian)  Name/ID:  

Questionnaire:

1. Age (between 40-80 years) or Date of birth
   Age:  Y:  M:  D:  

2. Sex
   Male  Female  

3. Weight (kg)  65  

4. Height (cm)  166.1  

5. Previous fracture
   No  Yes  

6. Previous fractured hip
   No  Yes  

7. Current smoking
   No  Yes  

8. Glucocorticoids
   No  Yes  

9. Rheumatoid arthritis
   No  Yes  

10. Secondary osteoporosis
    No  Yes  

11. Alcohol 3 or more units per day
    No  Yes  

12. Femoral neck BMD (g/cm²)
    GE-Lunar  0.725  T-score: -2.3  

BMI 23.8
The ten year probability of fracture (%) with BMD
- Major osteoporotic  22
- Hip fracture  2.4

Weight Conversion
Pounds  kg

Height Conversion
Inches  cm

Having trouble with the FRAX tool?
If you experience any problems with the FRAX tool please upgrade your version of Adobe Flash. Click here to upgrade.

For USA use only
Who to Treat?

- FDA approved medical therapies should be considered in post menopausal women and men age 50 and older with
  - A hip or vertebral (clinical or morphometric) fracture
  - T-score ≤ -2.5 at the femoral neck or spine after appropriate evaluation to exclude secondary causes
Who to Treat?

• Low bone mass (T-score between -1.0 and -2.5 at the femoral neck or spine) AND a 10-year probability of a hip fracture ≥ 3% OR a 10-year probability of a major osteoporosis-related fracture ≥ 20% based on the US-adapted WHO algorithm

• Clinician's judgment and/or patient preferences may indicate treatment for people with 10-year fracture probabilities above or below these levels
Universal Recommendations For All Patients To Reduce Fracture Risk

• Adequate calcium intake
• Adequate vitamin D intake
• Participation in weight bearing and muscle strengthening exercise
• Avoidance of tobacco use
• Avoidance and treatment of alcoholism
### TABLE 6. Estimating Daily Dietary Calcium Intake

**STEP 1: Estimate calcium intake from calcium-rich foods**

<table>
<thead>
<tr>
<th>Product</th>
<th>Servings/d</th>
<th>Estimated calcium/serving, in mg</th>
<th>Calcium, in mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milk (8 oz.)</td>
<td>_________</td>
<td>x 300</td>
<td>=</td>
</tr>
<tr>
<td>Yogurt (6 oz.)</td>
<td>_________</td>
<td>x 300</td>
<td>=</td>
</tr>
<tr>
<td>Cheese (1 oz. or 1 cubic in.)</td>
<td>_________</td>
<td>x 200</td>
<td>=</td>
</tr>
<tr>
<td>Fortified foods or juices</td>
<td>_________</td>
<td>x 80 to 1,000**</td>
<td>=</td>
</tr>
</tbody>
</table>

**STEP 2: Total from above + 250 mg for nondairy sources**

= total dietary calcium

Calcium, in mg

---

* About 75 to 80 percent of the calcium consumed in American diets is from dairy products.

** Calcium content of fortified foods varies.
Calcium Intake: Practical Points

- Supplements are only needed if the dietary calcium is inadequate.
- Aim for ~1000-1200 mg/day of total calcium.
- Divided doses for supplementation of >500 mg/day.
## Calcium Intake: Practical Points

<table>
<thead>
<tr>
<th></th>
<th>Calcium Citrate</th>
<th>Calcium Carbonate</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>With Food</strong></td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>With Proton pump inhibitors</strong></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td><strong>Elemental calcium</strong></td>
<td>20%</td>
<td>40%</td>
</tr>
</tbody>
</table>

---

*Calcium Citrate vs. Calcium Carbonate: Practical Considerations*
Weight Bearing Exercise

- Brisk walking, jogging, and hiking
- Yard work such as pushing a lawnmower and heavy gardening
- Team sports, such as soccer, baseball, and basketball
- Dancing, step aerobics, and stair climbing
- Tennis and other racquet sports
- Skiing, skating, karate, and bowling
- Weight training with free weights or machines

- Consider referrals for physical and/or occupational therapy evaluation
Pharmacological Treatment
US FDA Approved Drugs For Post- Menopausal OP (√) and OP in Men (M)

<table>
<thead>
<tr>
<th>Bisphosphonate (BP)</th>
<th>Prevention</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alendronate</td>
<td>√</td>
<td>√ (M)</td>
</tr>
<tr>
<td>Alendronate + D</td>
<td>√</td>
<td></td>
</tr>
<tr>
<td>Risedronate</td>
<td>√</td>
<td>√ (M)</td>
</tr>
<tr>
<td>Ibandronate</td>
<td>√</td>
<td>√</td>
</tr>
<tr>
<td>Zoledronic acid</td>
<td>√</td>
<td>√ (M)</td>
</tr>
</tbody>
</table>
Drug Safety

- Difficulty swallowing, esophageal inflammation and gastric ulcer
- Reduction of GFR
- Osteonecrosis of jaw
- Eye inflammation
- Low trauma atypical subtrochanteric and diaphyseal femoral fractures
- IV BPs
  - Acute phase reaction
### US FDA Approved Drugs For Post-Menopausal OP (√) and OP in Men (M)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Prevention</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcitonin</td>
<td></td>
<td>√</td>
</tr>
<tr>
<td>Estrogen and/or Hormone Rx</td>
<td>√</td>
<td></td>
</tr>
<tr>
<td>Estrogen agonist/antagonist (raloxifene)</td>
<td>√</td>
<td>√</td>
</tr>
<tr>
<td>Parathyroid hormone [PTH (1, 34)]</td>
<td></td>
<td>√ (M)</td>
</tr>
<tr>
<td>Denosumab</td>
<td></td>
<td>√ (M)</td>
</tr>
</tbody>
</table>
Parathyroid Hormone : Teriparatide

• Efficacy after 18 months of therapy
  – Reduces risk of vertebral fractures by 65%
  – Reduces risk of non-vertebral fractures by 53%

• Drug administration
  – Anabolic 20 mcg SC
  – Bone loss is rapid after treatment is stopped
  – Alternative agents should be considered to maintain BMD

• Drug safety
  – Side effects: leg cramps, nausea, dizziness
  – Warning: Osteosarcoma rats, therefore cannot be used in Pagets, prior radiation therapy to skeleton, bone mets, hypercalcemia, h/o skeletal malignancy
RANK Ligand Inhibitor: Denosumab

• Efficacy after 3 years of therapy
  – Reduces risk of vertebral fractures by 68%
  – Reduces risk of hip fracture by 40%
  – Reduces risk of non-vertebral fractures by 20%

• Drug Administration
  – 60 mg SC every 6 months by health professional
  – Bone loss can be rapid after treatment is stopped
  – Alternative agents should be considered to maintain BMD

• Drug safety
  – Hypocalcemia
  – Increases risk of serious skin infections (cellulitis) and skin rash
  – Associated with osteonecrosis of jaw and atypical femur fractures
Monitoring Effectiveness Of Treatment

• Assess adherence

• Measuring biochemical markers of bone turnover
  – Urine and serum NTX
  – Serum CTX
  – Bone specific alkaline phosphatase

• Serial BMD
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