Secondary Causes of Osteoporosis:

What are they and when do I search for them?
Definitions

• **Primary osteoporosis**
  bone loss due to normal aging and natural menopause

• **Secondary osteoporosis**
  bone loss due to or made worse by a systemic disease, drug, or co-existing condition
Looking at the bone density

• T score: standard deviation from zero (peak bone density in 30 year old) gender matched and race matched
  – Minus 2.5 or worse is osteoporosis

• Z score: standard deviation from zero (age matched, gender matched and race matched)
  – Minus 2.0 or worse is a red flag for a work up.
Patient (indicated by *) has bone density 1 SD below age-matched normals and 2.5 below the mean bone density of young normals. Based on the WHO’s definition, this patient has osteoporosis.
Causes of Secondary Osteoporosis

- **Endocrine**
  - Hypogonadism
    - Athletic amenorrhea
    - Premature menopause
    - Anorexia nervosa*
    - Turner’s and Klinefelter’s syndromes
    - GnRH therapy (prostate cancer, endometriosis)
    - Testicular failure
    - Hypopituitarism
    - Hyperprolactinemia

* additional problems
Secondary causes: endocrine continued

- Diabetes mellitus type 1
- Cushing’s syndrome/steroid excess
- Hyperthyroidism
Secondary causes of osteoporosis

• Abnormal calcium balance
  vitamin D deficiency *
  hyperparathyroidism
  idiopathic hypercalciuria
  low calcium intake
Secondary causes of Osteoporosis

• **Genetic**
  – Osteogenesis imperfecta
  – Ehler’s-Danlos
  – Marfan syndrome
  – Homocystinuria
  – Hypophosphatiasia
  – Porphyria
  – Cystic fibrosis*
  – Hemochromatosis

these may cause failure to reach peak bone mass, accelerated bone loss, and fractures.
Secondary Causes of Osteoporosis

• **Gastrointestinal**
  – Celiac disease *
  – Bariatric Surgery *
  – Post-gastrectomy
  – Inflammatory bowel disease
  – Malabsorption
  – Primary Biliary cirrhosis
  – End-stage renal disease

*GI symptoms may be minor, bone loss and/or fx may be prominent or presenting symptom
Secondary Causes of Osteoporosis

- **Hematologic**
  - Multiple myeloma*
  - Sickle-cell disease
  - Thalassemia
  - Hemophilia
  - Leukemias
  - Lymphomas
  - Systemic mastocytosis
Secondary Causes of Osteoporosis

• Rheumatologic
  – Ankylosing spondylitis
  – Rheumatoid arthritis
Secondary Causes of Osteoporosis

- **Drugs**
  - Glucocorticoids*
  - Suppressive doses of thyroid hormone
  - Anticonvulsants (phenytoin, phenobarbital)
  - Heparin
  - GnRH analogues (leuprolide)
  - Immunosuppressants (cyclosporine, tacrolimus)
  - Cytotoxic drugs (methotrexate)
Secondary Causes of Osteoporosis

- Miscellaneous
  - Alcoholism*
  - Organ transplantation*
  - Emphysema/COPD
  - End-stage renal disease
  - Idiopathic scoliosis
  - Immobilization
  - some of these are very common!!
How common is secondary osteoporosis?

- More likely to find a cause in men and pre-menopausal women
- Any age group - important consideration
- Changes the management

Prevalence in Men: 50-80%
Prevalence in post menopausal women: about 30%
Who to work up?

- All men with low T-scores and/or fragility fractures
- Women:
  - Pre-menopausal with low z-score and/or fragility fractures
  - Post-menopausal with z-score less than minus 2 or fractures or as clinical judgment dictates

Men or Women: if they are on effective therapy but losing bone or fracturing.
What is a fragility fracture?

- A low intensity, non traumatic fracture that occurs spontaneously or due to a fall from a standing position or less.
- Does not include face, finger and foot fractures
What evaluation to perform?

- **History**
  - Any fractures after age 45?
  - Age at menopause?
  - Any HRT/ERT after menopause?
  - Mother have a hip fracture?
  - Lifetime calcium intake?
  - Malabsorption/GI disease?
  - Drugs: prednisone, anti-seizure meds, aromatase inhibitors, chemotherapy
  - Chronic diseases
What evaluation to perform?

• Physical exam
  – Height and weight!
  – Appearance?
  – Palpate thyroid gland. Normal is 20 g or less and without nodules
  – Look for kyphosis and scoliosis
  – Any tremor, sweating or proptosis?
  – Any bruising, striae or liver enlargement?
  – Any ankle swelling
  – Can they get up from their chair without using their arms?
  – Is their gait stable?
What Evaluation to Perform?

Laboratory testing

- Serum calcium, phosphorus, albumin, creatinine
- Parathyroid hormone (PTH)
- TSH
- SGOT
- CBC
- 24 hour urine for calcium and creatinine
- 25 OH vitamin D
- Testosterone (men) 7 AM total Testosterone please
Further lab testing

• Be selective!
  – SPEP, UPEP
  – Antigliadin, antiendomyseal antibodies (Celiac)
  – Consult if you think Cushing’s/Klinefelter’s
Most prevalent lab abnormalities

- Vitamin D deficiencies: 6 - 39%
- Elevated PTH: 1 - 15%
- Hypercalciuria:
  - 7% - 9.8% in women
  - 20 - 41% in men
- Hyperthyroidism: 2.5 - 7.5%
- Malabsorption: 7%
Vitamin D deficiency

• Definition of sufficiency controversial: thought that pt needs 25 hydroxy vitamin D concentration of:
  – 20 ng/ml for normal PTH dynamics
  – 32-36 ng/ml for max intestinal Ca++ transport
  – 30-40 ng/ml for fracture reduction
Treatment of Vitamin D insufficiency

If vitamin D level is very low (under 20) and patient is healthy and young:

give 50,000 international units daily for one week and then weekly for two months.

check the creatinine and calcium at two weeks and then monthly. Reassess at two months.
Treatment of vitamin D deficiency

• If the patient has a low vitamin D and is healthy and has symptoms (myalgias and weakness)
  – Clinical judgment required:
    • 50,000 international units daily for one week and then weekly for two months.
    • OR
    • 50,000 international units weekly for two months
The need to monitor

• Whenever you use large doses of vitamin D you need to check the serum creatinine and serum calcium two weeks after starting therapy and then monthly.
Treatment of vitamin D deficiency

• If the patient is elderly or has an elevated creatinine or chronic kidney disease:
  – 1200 international units of vit D daily is reasonable. No need to monitor unless elevated creatinine. May need to check with nephrologist.
  – May have to treat for 6 months to one year.
Secondary Causes of Osteoporosis: Conclusions

- They are frequent: especially vitamin D insufficiency or deficiency
- Multiple systems contribute to bone health and bone disease.
  - **good History and Physical are essential!! Important to consider as these diagnoses will change the management
Secondary Causes of Osteoporosis: Conclusions

• Many things can be contributing: ask the questions and do the labs!
  – Don’t forget men!
  – Pre-menopausal women with low Z score
  – Postmenopausal women with low Z score (minus 2.0 or lower)