

## Secondary Causes of Osteoporosis: Invisible or Hidden in Plain Sight?

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## The Reflex

- Postmenopausal woman with low BMD
- ↓
- Treat with a medication for osteoporosis

## Risk Factors for Osteoporotic Fracture

- Low Bone Mass
- Personal History of Fracture
- Family History of Fracture
- Smoking
- Low Body Weight

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- Low Bone Mass
- Personal History of Fracture
- Family History of Fracture
- Smoking
- Low Body Weight
- Age and Sex
- Falls

## The Problem

- There are many disorders that cause or contribute to low bone density
- Who needs to be evaluated for these disorders before treatment with osteoporosis medications is initiated?
- What disorders are common and what should receive our attention in this evaluation?

## The Obvious Case

- 49 year old African American woman found to have low BMD (LS T -3.9)
- Treated with Fosamax
- Two years later, BMD decreased 4.3%
- Hypertension, weight gain
- Urine cortisol and overnight dexamethasone suppression abnormal

## Case 2

- 57 year old white male
- Fx metatarsals 6 years ago
- Pain R hip, "insufficiency fracture femur"
- BMD LS: + 5.6, TH: + 1.1, FN: + 0.1
- Laboratory testing:
  - Calcium 8.9, Alk Phos 185, PTH 47
  - 25OH vitamin D 21.5 ng/ml (8.9-46.7)
  - Phosphorus 1.4

## Case 2

- 57 year old white male
- Phosphorus 1.4
- Acquired hypophosphatemic osteomalacia



## Case 3

- 70 year old white female
- Menopause at age 50, on estrogen for 5 years, then stopped
- Non-smoker, weight 140 lbs, no other symptoms, no known height loss
- BMD LS: - 2.5, TH: - 2.7, FN: - 2.9

## Conditions Associated with Increased Risk for Osteoporosis (NOF)

AIDS/HIV	Hyperparathyroidism	Multiple Sclerosis
Amyloidosis	Hypogonadism (primary or secondary)	Multiple Myeloma
Ankylosing Spondylitis	Hypophosphatasia	Pernicious Anemia
COPD	Hypophosphatemia	Rheumatoid Arthritis
Congenital Porphyria	Idiopathic Scoliosis	Severe Liver Disease, esp PBC
Cushings Syndrome	Inadequate Diet	Spinal Cord Injury
Eating Disorders	Inflammatory Bowel Disease	Sprue
Female Athlete Triad	Insulin-Dependent Diabetes	Stroke/CVA
Gastrectomy	Lymphoma/Leukemia	Thalassemia
Gaucher's Disease	Malabsorption Syndromes	Thyrototoxicosis
Hemochromatosis	Mastocytosis	Tumor
Hemophilia		Weight Loss

NOF Physician's Guide

## Secondary Causes of Low Bone Mass in Adults

Inherited	Nutritional	Endocrine	Other
Osteogenesis imperfecta	Malabsorption	Hypogonadism	Rheumatoid Arthritis
Homocystinuria	Eating Disorders	Thyrototoxicosis	Immobilization
Marfan Syndrome	Female Athlete Triad	Glucocorticoid Excess	Myeloma
Osteoporosis / Pseudoglioma syndrome	Alcoholism	Hyperparathyroidism	Mastocytosis
	Chronic Liver Disease		Osteomalacia
	Vitamin D Deficiency		
	Calcium Deficiency		

## Drugs associated with an increased risk for reduced bone mass....

- Aluminum
- Anticonvulsants
- Aromatase inhibitors
- Cytotoxic drugs
- Glucocorticoids/ACTH
- GnRH agonists/analogs
- Immunosuppressants
- Lithium
- Long-term heparin
- Depo-progesterone
- Supraphysiologic thyroxine replacement
- Tamoxifen (premenopausal use)
- Total parenteral nutrition

From NOF Physician's Guide

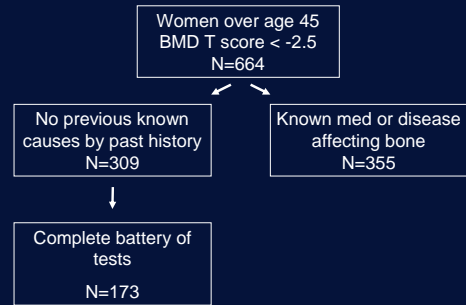
## In evaluating patients with osteoporosis, what needs our attention?

### Yield of Laboratory Testing to Identify Secondary Contributors to Osteoporosis in Otherwise Healthy Women

CARA TANNENBAUM, JULIE CLARK, KEVIN SCHWARTZMAN, SYLVAN WALLENSTEIN, ROBERT LAPINSKI, DIANE MEIER, AND MARJORIE LUCKEY

The Journal of Clinical Endocrinology and Metabolism, 87: 4431-4437, 2002

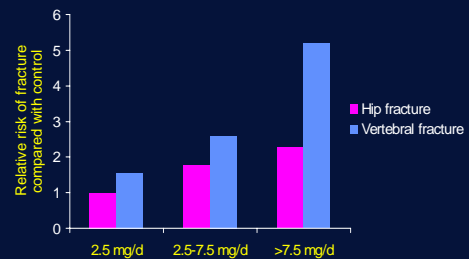
## Study Design



## Exclusions by Medical History N = 355

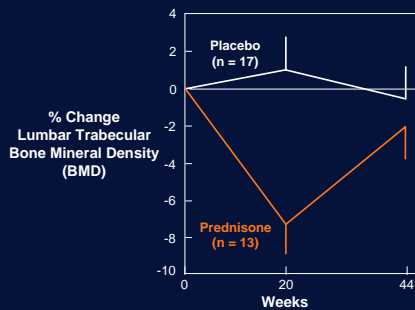
- Oral glucocorticoid treatment 36%
- Premature ovarian failure 21
- Malnutrition 10
- Alcoholism 10
- Liver disease 10
- Immobilization > 3 months 9
- Systemic chemotherapy 8
- History of hyperthyroidism 6
- Anticonvulsant use 5
- RA or SLE 5
- Hyperparathyroidism 5
- Intestinal Malabsorption 4
- Other known disorder or medication 6

## Fracture Risk and Dose of Corticosteroids



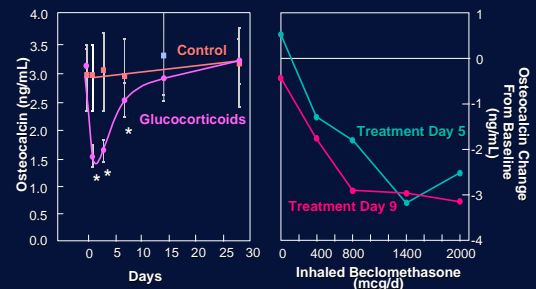
Relative risk of fracture by dosages of corticosteroids of prednisolone. van Staa TP, et al, 1998.

## Rapid BMD Decline Due to Glucocorticoids in Rheumatoid Arthritis



Laan R. Ann Intern Med. 1993;119:966.

## Effects of Inhaled and Intra-Articular Glucocorticoids on Bone Is There a Safe Dose?



Emkey RD. Arthritis Rheum. 1990;39:277.

Teelucksingh S. Lancet. 1991;338:61.

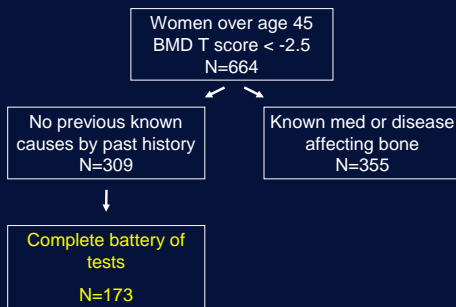
Recommendations for the Prevention and Treatment of  
Glucocorticoid-Induced Osteoporosis

--Arthritis and Rheumatism 44:1496-1503, 2001

Recommendations for the Prevention and Treatment of  
Glucocorticoid-Induced Osteoporosis

- Minimize steroid dose
- Calcium and vitamin D
- Bisphosphonate (risedronate, alendronate)
- Monitor
  - BMD
  - Urine calcium

Study Design



Disorders Discovered by Testing  
N = 173

- |                               |   |    |
|-------------------------------|---|----|
| • Exogenous hyperthyroidism   | 4 | 2% |
| • Cushings disease            | 1 | 1% |
| • Primary hyperparathyroidism | 1 | 1% |
| • Hypocalciuric hypercalcemia | 1 | 1% |

Disorders Discovered by Testing  
N = 173

- |                               |           |            |
|-------------------------------|-----------|------------|
| • Exogenous hyperthyroidism   | 4         | 2%         |
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| • Primary hyperparathyroidism | 1         | 1%         |
| • Hypocalciuric hypercalcemia | 1         | 1%         |
| • <b>Hypercalciuria</b>       | <b>17</b> | <b>10%</b> |

Disorders Discovered by Testing  
N = 173

- |                                       |    |     |
|---------------------------------------|----|-----|
| • Exogenous hyperthyroidism           | 4  | 2%  |
| • Cushings disease                    | 1  | 1%  |
| • Primary hyperparathyroidism         | 1  | 1%  |
| • Hypocalciuric hypercalcemia         | 1  | 1%  |
| • Hypercalciuria                      | 17 | 10% |
| • Malabsorption                       | 14 | 8%  |
| • Celiac disease (3)                  |    |     |
| • Calcium malabsorption (11)          |    |     |
| • Secondary hyperparathyroidism       | 11 | 6%  |
| • "inadequate calcium" (6)            |    |     |
| • "unexplained" (5)                   |    |     |
| • Vitamin D deficiency (< 12.5 ng/ml) | 7  | 4%  |

### Disorders Discovered by Testing N = 173

• Exogenous hyperthyroidism	4	2%
• Cushings disease	1	1%
• Primary hyperparathyroidism	1	1%
• Hypocalciuric hypercalcemia	1	1%
• Hypercalciuria	17	10%
• Malabsorption	14	8%
• Celiac disease (3)		
• Calcium malabsorption (11)		
• Secondary hyperparathyroidism	11	6%
• "inadequate calcium" (6)		
• "unexplained" (5)		
• Vitamin D deficiency (< 20 ng/ml)	36	21%

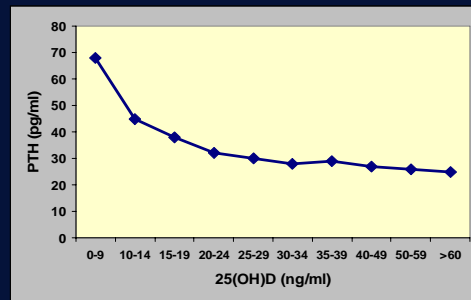
### Disorders Discovered by Testing N = 173

• Exogenous hyperthyroidism	4	2%
• Cushings disease	1	1%
• Primary hyperparathyroidism	1	1%
• Hypocalciuric hypercalcemia	1	1%
• Hypercalciuria	17	10%
• Malabsorption	14	8%
• Celiac disease (3)		
• Calcium malabsorption (11)		
• Secondary hyperparathyroidism	11	6%
• "inadequate calcium" (6)		
• "unexplained" (5)		
• Vitamin D deficiency (< 20 ng/ml)	36	21%
• Patients with a new diagnosis		49%

### Disorders Discovered by Testing N = 173

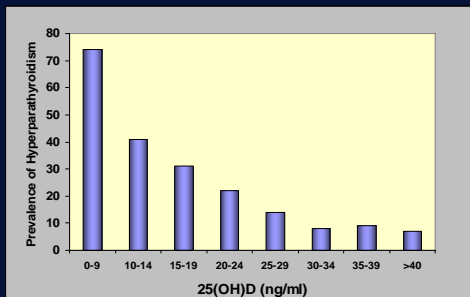
• Vitamin D deficiency		
• < 12.5 ng/ml	7	4%
• < 20.0 ng/ml (+29)	36	21%
• < 32.0 ng/ml (+55)	91	53%

### Mean PTH Concentrations

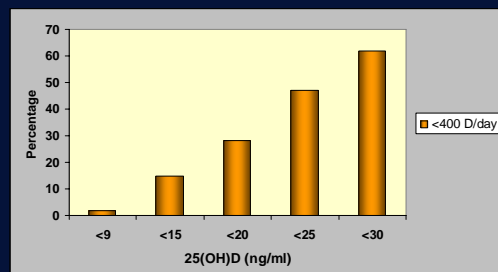


Holick, et al JCEM, 2005

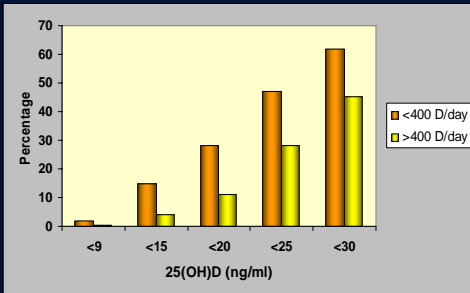
### Prevalence of Elevated PTH



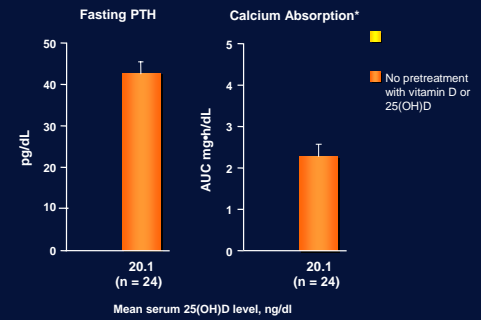
### Population Distribution of Vitamin D Levels



## Population Distribution of Vitamin D Levels

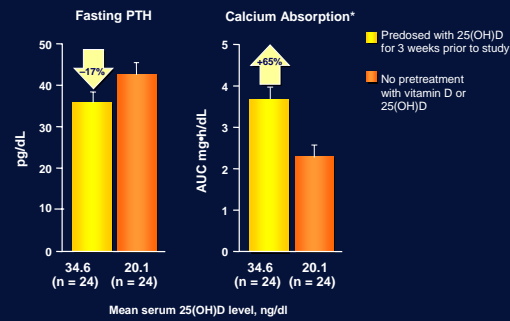


## Vitamin D Status: Impact on Calcium Absorption and PTH



Heaney RP et al. J Am Coll Nutr. 2003;22:142-146.

## Vitamin D Status: Impact on Calcium Absorption and PTH



Heaney RP et al. J Am Coll Nutr. 2003;22:142-146.

## Fracture Prevention With Vitamin D Supplementation

A Meta-analysis of Randomized Controlled Trials

Heike A. Bischoff-Ferrari, MD, MPH  
 Walter C. Willett, DrPH  
 John B. Wong, MD  
 Edward Giovannucci, ScD  
 Thomas Dietrich, MPH  
 Bess Dawson-Hughes, MD

JAMA. 2005;293:2257-2264

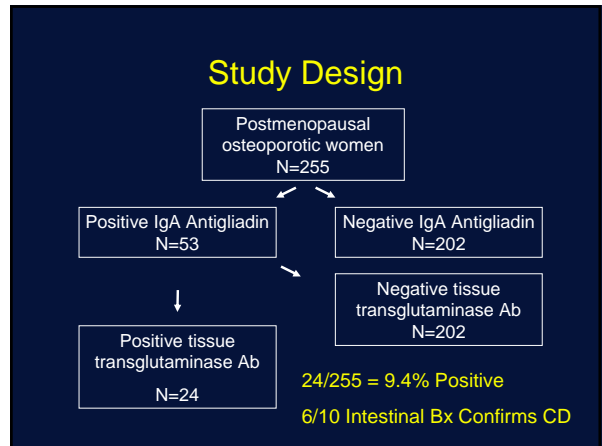
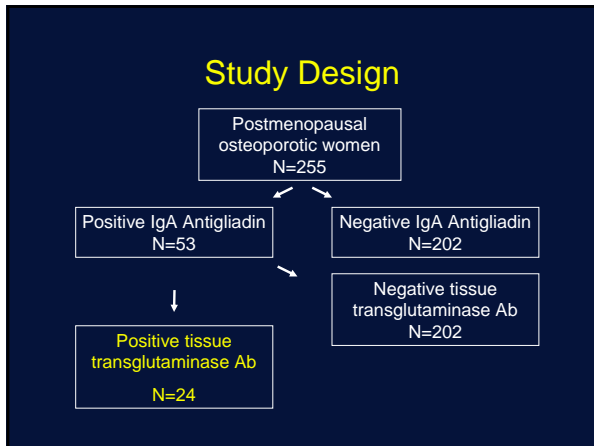
## Prevalence of undiagnosed coeliac syndrome in osteoporotic women

R. NUTI, G. MARTINI, R. VALENTI, S. GIOVANI, S. SALVADORI & A. AVANZATI  
 From the Institute of Internal Medicine, Metabolic Disease Unit, University of Siena, Siena, Italy

Journal of Internal Medicine 250:361-366, 2001

## Study Design

Postmenopausal  
 osteoporotic women  
 N=255



- ### In evaluating patients with osteoporosis, what needs our attention?
- Many patients with low bone mass have identifiable abnormalities
  - Patients with osteoporosis should have a comprehensive evaluation
    - History and Physical Examination
    - Chemistry Panel including Phosphorus
    - 24 hour urine calcium, 25OHD, PTH
    - TSH for patients on thyroid hormone or with symptoms

- ### In evaluating patients with osteoporosis, what needs our attention?
- Many patients with low bone mass have identifiable abnormalities
  - Patients with osteoporosis should have a comprehensive evaluation
  - **Greater emphasis should be placed on adequate calcium and vitamin D nutrition**

