

EVALUATION FOR SECONDARY CAUSES OF FRACTURES

DR. IRINEL STANCIU, MD, FACE, CCD, ECNU

FEEL BETTER. DO MORE.

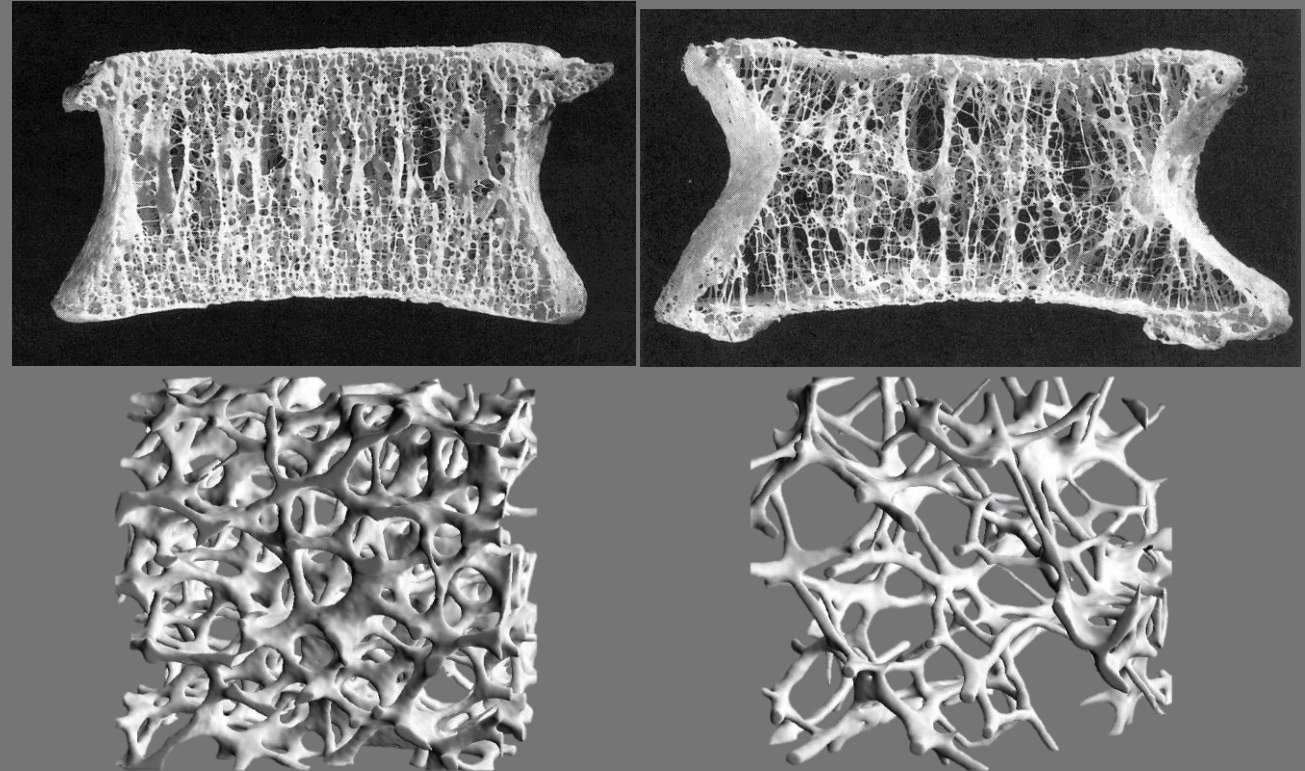
DISCLOSURES



- Member of speaker bureau for Radius Health and Alexion Pharmaceuticals
- Scientific advisory board for Ultragenyx
- Principal investigator for research trials with Radius and Ultragenyx (research funds received by Panorama)

OSTEOPOROSIS = **LOW BONE MASS** AND **MICROARCHITECTURE DETERIORATION**

“A systemic skeletal disease characterized by **low bone mass** and **microarchitectural deterioration** of bone tissue with a consequent increase in bone fragility and susceptibility to fracture.”



*Consensus Development Conference: Diagnosis, Prophylaxis, and Treatment of Osteoporosis. Am J Med. 1991;90:107- d

WHO CLASSIFICATION OF OSTEOPOROSIS

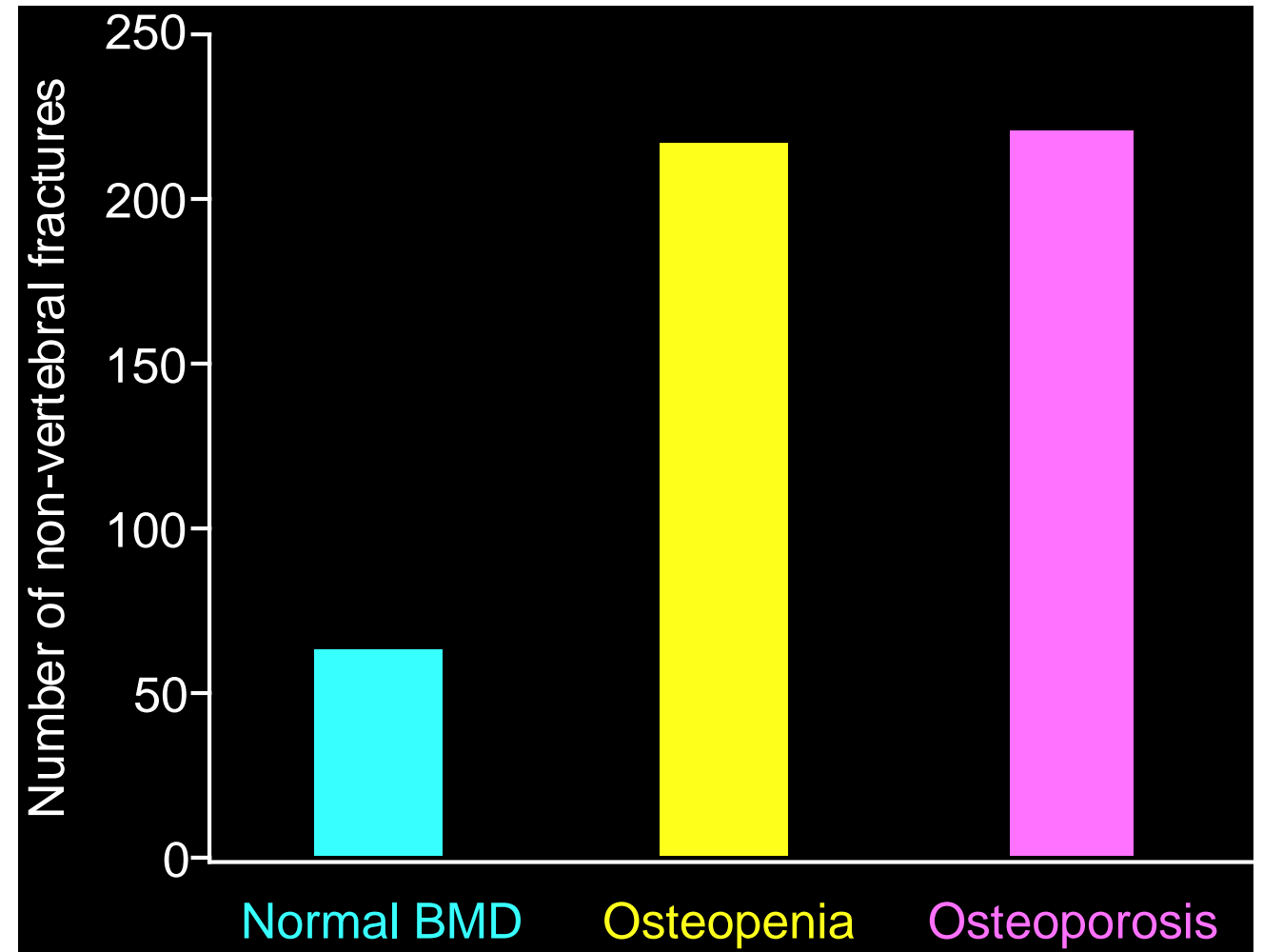
| CLASSIFICATION | T-SCORE |
|-------------------------------|---|
| NORMAL | - 1.0 OR GREATER |
| LOW BONE MASS (OSTEOPENIA) | BETWEEN - 1.0 AND - 2.5 |
| OSTEOPOROSIS | - 2.5 AND BELOW |
| SEVERE OSTEOPOROSIS | - 2.5 AND BELOW + FRAGILITY FRACTURE |

For peri and postmenopausal females and men over age 50

**NOT EVERY LOW T-SCORE IS
OSTEOPOROSIS**

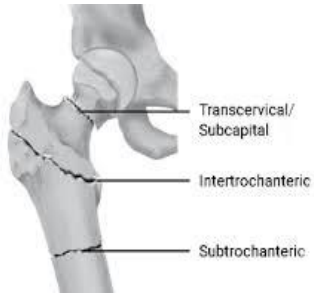
**MORE PEOPLE WITH NON-
OSTEOPOROTIC
T-SCORES HAVE FRACTURES**

**USING T-SCORE
ALONE
IDENTIFIES < 50%
OF WOMEN AND
~25% OF MEN
WHO WILL
FRACTURE**



LOW TRAUMA FRACTURE = BONE ATTACK

Fracture = Clinical Osteoporosis



Vertebral Fragility Fractures (VFF)

Normal



Kyphotic



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AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS/ AMERICAN COLLEGE OF ENDOCRINOLOGY CLINICAL PRACTICE GUIDELINES FOR THE DIAGNOSIS AND TREATMENT OF POSTMENOPAUSAL OSTEOPOROSIS— 2020 UPDATE

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Q2. WHEN OSTEOPOROSIS IS DIAGNOSED WHAT IS AN APPROPRIATE EVALUATION?

- **R7.** Evaluate for causes of secondary osteoporosis (**Grade B; BEL 1, downgraded due to limited evidence**).
- **R8.** Evaluate for prevalent vertebral fractures (**Grade B; BEL 2**).
- **R9.** Consider using bone turnover markers in the initial evaluation and follow-up of osteoporosis patients. Elevated levels can predict more rapid rates of bone loss and higher fracture risk (**Grade A; BEL 1**).

Table 12
Causes of Secondary Osteoporosis in Adults^a

| Endocrine or metabolic causes | Nutritional/ GI conditions | Drugs | Disorders of collagen metabolism | Other |
|--|--|--|--|--|
| Acromegaly Diabetes mellitus Type 1 Type 2 Growth hormone deficiency Hypercortisolism Hyperparathyroidism Hyperthyroidism Hypogonadism Hypophosphatasia Porphyria Pregnancy | Alcoholism Anorexia nervosa Calcium deficiency Chronic liver disease Malabsorption syndromes/ malnutrition (including celiac disease, cystic fibrosis, Crohn disease, and gastric resection or bypass) Total parenteral nutrition Vitamin D deficiency | Anti-epileptic drugs ^b Aromatase inhibitors Chemotherapy/ immunosuppressants Medroxyprogesterone acetate Glucocorticoids Gonadotropin-releasing hormone agents Heparin Lithium Proton pump inhibitors Selective serotonin- reuptake inhibitors SGLT2-inhibitors Thiazolidinediones Thyroid hormone (in supraphysiologic doses) | Ehlers-Danlos syndrome Homocystinuria due to cystathionine deficiency Marfan syndrome Osteogenesis imperfecta | AIDS/HIV Ankylosing spondylitis Chronic obstructive pulmonary disease Gaucher disease Hemophilia Hypercalciuria Immobilization Major depression Myeloma and some cancers Organ transplantation Renal insufficiency/failure Renal tubular acidosis Rheumatoid arthritis Systemic mastocytosis Thalassemia |

AIDS = acquired immunodeficiency syndrome; GI = gastrointestinal; HIV = human immunodeficiency virus; SGLT2 = sodium-glucose cotransporter 2.

^aNot meant to be a complete list.

^bPhenobarbital, phenytoin, primidone, valproate, and carbamazepine have been associated with low bone mass.

Table 13
Laboratory Tests to Consider in Detecting Secondary Osteoporosis

Complete blood cell count
 Serum chemistry, including calcium, phosphate, total protein, albumin, liver enzymes, alkaline phosphatase, creatinine, and electrolytes
 24-hour collection for calcium, sodium, and creatinine excretion (to identify calcium malabsorption or hypercalciuria)
 Serum 25-hydroxyvitamin D

Additional tests if clinically indicated might include (but not limited to):

- Serum intact parathyroid hormone concentration for possible primary or secondary hyperparathyroidism
- Serum thyrotropin
- Tissue transglutaminase antibodies for suspected celiac disease
- Serum protein electrophoresis and free kappa and lambda light chains for suspected myeloma
- Urinary free cortisol or other tests for suspected adrenal hypersecretion
- Serum tryptase, urine N-methylhistidine, or other tests for mastocytosis
- Bone marrow aspiration and biopsy to look for marrow-based diseases
- Undecalcified iliac crest bone biopsy with double tetracycline labeling

Recommended for patients with bone disease and renal failure to establish the correct diagnosis and direct management

May be helpful in the assessment of patients with the following:

Suspected osteomalacia or mastocytosis when laboratory test results are inconclusive

Fracture without major trauma despite normal or high bone density

Vitamin D–resistant osteomalacia and similar disorders to assess response to treatment

Genetic testing for unusual features that suggest rare metabolic bone diseases



UP TO 30% OF POST-MENOPAUSAL WOMEN
AND 50-80% OF MEN SUFFER FROM
DISEASES OR HAVE FACTORS
CONTRIBUTING TO OSTEOPOROSIS

*NIH. Consensus Development Panel on Osteoporosis Prevention D Therapy. Osteoporosis prevention, diagnosis, and therapy. JAMA **2001**, 285, 785–795.*

*Mirza, F.; Canalis, E. Management of endocrine disease: Secondary osteoporosis: Pathophysiology and management. Eur. J. Endocrinol. **2015**, 173, R131–R151.*



SPECIAL FEATURE

Clinical Practice Guideline

Osteoporosis in Men: An Endocrine Society Clinical Practice Guideline

Nelson B. Watts, Robert A. Adler, John P. Bilezikian, Matthew T. Drake, Richard Eastell, Eric S. Orwoll, and Joel S. Finkelstein

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Clinician's Guide to Prevention and Treatment of Osteoporosis

F. Cosman • S. J. de Beur • M. S. LeBoff • E. M. Lewiecki •
B. Tanner • S. Randall • R. Lindsay

- Metabolic bone diseases other than osteoporosis (hyperparathyroidism, osteomalacia) may be associated with low BMD.
- Many of these diseases have very specific therapies, and it is appropriate to complete a history and physical examination **before making a diagnosis of osteoporosis** on the basis of a low BMD alone.
- In patients in whom a specific secondary, treatable cause of osteoporosis is being considered relevant blood and urine studies should be obtained prior to initiating therapy.

MEDICATIONS THAT CAUSE OR CONTRIBUTE TO OSTEOPOROSIS AND FRACTURES

Aluminum (in antacids)
Aromatase inhibitors
Depo-medroxyprogesterone
(premenopausal contraception)
Lithium
Cyclosporine A
Tacrolimus
Proton pump inhibitors
Tamoxifen® (premenopausal
use)
Anticoagulants (heparin)
Barbiturates

Glucocorticoids (≥ 5 mg/day prednisone or
equivalent for ≥ 3 months)
Methotrexate
Selective serotonin reuptake inhibitors
Thiazolidinediones
Excess vitamin A
Anticonvulsants
Cancer chemotherapeutic drugs
GnRH (gonadotropin-releasing hormone) agonists
Parental nutrition
Thyroid hormones (in excess)

IT IS IMPORTANT TO KNOW AND TREAT THE UNDERLYING CAUSE IN ORDER TO REDUCE FRACTURE RISK



Alendronate has a reduced efficacy in post-menopausal women with osteoporosis receiving thyroid-stimulating hormone (TSH)-suppressive doses of levothyroxine (L-T4) for the management of differentiated carcinoma of the thyroid

SECONDARY HYPERPARATHYROIDISM NON-RENAL - BARIARIC SURGERY

- 21.0% prevalence **before surgery** - not different between different bariatric procedures.
- 35.4% at 1 year after surgery
- 63.3% at 5 years after surgery

| | 1 YR (%) | 5 YRS (%) |
|------|----------|-----------|
| SAGB | 50.6 | 73.6 |
| RYGB | 33.2 | 56.6 |
| LAGB | 25.8 | 38.5 |
| SG | 17.8 | 41.7 |

Roux-en-Y gastric bypass = RYGB; single anastomosis (mini-) gastric bypass = SAGB; laparoscopic adjustable gastric banding = LAGB; sleeve gastrectomy (SG).

SECONDARY HYPERPARATHYROIDISM NON-RENAL - CELIAC DISEASE (CD)

- The presentation of CD has been changing, with a shift toward older individuals with more mild disease
- Subclinical and nonclassical cases now make up 30-60% of new cases
- Diagnosis relies on serology tests, but confirmation with intestinal biopsies is required.
- 40-70% prevalence of low bone mineral density in CD
- Osteoporotic fractures accounts for 2.8 million disability-adjusted life years annually

Hujoel IA, Reilly NR, Rubio-Tapia A. Celiac Disease: Clinical Features and Diagnosis. *Gastroenterol Clin North Am.* 2019;48(1):19-37.

Ludvigsson JF, Murray JA. Epidemiology of Celiac Disease. *Gastroenterol Clin North Am.* 2019;48(1):1-18.

Ganji R, Moghbeli M, Sadeghi R, Bayat G, Ganji A. Prevalence of osteoporosis and osteopenia in men and premenopausal women with celiac disease: a systematic review. *Nutr J.* 2019;18(1):9.

Published 2019 Feb 7.

METABOLIC BONE WORK-UP IN CCBP

EVERY PATIENT

- CBC, CMP I4, PHOSPHORUS
- PTH, 25OH VITAMIN D
- 24H URINE CALCIUM, SODIUM, CREATININE
- CELIAC SCREEN
- SPEP/IFE & FREE LIGHT CHAIN RATIO
- ESR
- CTX
- BSAP
- PINP, OC

AS INDICATED BY HISTORY OR INITIAL W/UP

- TSH, FREE T4
- 24H URINE FREE CORTISOL, CREATININE
- TRYPTASE
- VITAMIN B6, 24h UR PEA
- 1,25 DI (OH) VITAMIN D
- PTHrp
- Genetic tests

CASE #1

- 54 y old F, menopausal
- Never smoker
- **6/2018 Back pain after shoveling rocks**
- Xray: L1,2,3,5 VCFx
- MRI confirmed L1,3 VCF
- Schmorl nodes L5
- Decreased T1 marrow signal (red marrow expansion)
- Ortho- conservative Tx
- **10/2018 - hematology eval**
- unprovoked DVT
- Iron deficiency anemia
- SPEP negative
- GI w/up negative including celiac
- Tx- iron infusions

ENDOCRINE W/UP

| | BMD (g/cm ²) | T-score |
|---------|--------------------------|---------|
| LI-L4 | 1.028 | - 1.3 |
| LFN | 0.853 | - 1.3 |
| LTH | 0.938 | - 0.6 |
| RFN | 0.777 | - 1.9 |
| RTH | 0.897 | - 0.9 |
| I/3 rad | 0897 | + 0.1 |

TBS LI-L4 = 1.117 (low)
TBS adj T-score = - 2.6

- 25OHD = 45
- **Ca = 10.2; PTH = 7.1**
- Creat = 0.6, Phos = 4.3
- 24h UR Ca = 608 mg; vol 2250 mL
- Liver, thyroid normal

10/2018 DXA GE Lunar

ONE YEAR LATER - SEPTEMBER 2019

- Multiple VCFx: T3,6,7,8,9,10,11,12; L1,3,4
- One episode nephrolithiasis
- **Meds:** HCTZ, Xarelto, iron, Cymbalta, Celebrex, Flexeryl, Calcium, MVI
- IgA 16 (87-352);
- tTG IgA and IgG negative
- **SPEP:** IgG 480 (700-1600); IgM = 19 (26-217); **M-spike neg**
- 25OHD = 105;
- Ca= 10; PTH 11
- phos = 4.6; creatinine = 0.64
- BSAP=17.7
- CTX=1131;
- OC=9.7; PINP=71

FURTHER W/UP

- Calcium, MVI, vitamin D stopped
- **CT urogram:** marked diffuse soft tissue replacement of normal fatty marrow throughout the axial skeleton with numerous areas of cortical destruction and marked osteoporosis. **Advanced myeloproliferative disorder is strongly suspected.**
- Bone marrow biopsy: plasma cell malignancy Kappa chain restricted consistent with **non-secretory multiple myeloma**

REMEMBER

- Hypercalciuria can be very common in the absence of nephrolithiasis
- 24h urine calcium/creat (or stone risk), PTH and CT urogram are necessary
- MGUS and MM are not very rare
- Abnormal SPEP (even with M-spike negative) should be referred to hematology
- Multiple compression fractures - look for a secondary cause (MM, Denosumab discontinuation, Cushing Sd)

HEMATOLOGICAL DISEASES AND OSTEOPOROSIS

- **MGUS and MM**, systemic mastocytosis, thalassemia major, sickle cell disease, and hemophilia - most evidence of affecting bone health
- **Close relationships between bone and bone marrow** - bone cells interact with hematopoietic cells, providing a supportive microenvironment needed to maintain erythropoiesis and myelopoiesis
- **Cytokines** can alter bone turnover, increasing the activity of osteoclasts and/or reducing the action of osteoblasts.
- **Hypoxia** is a potent stimulator of erythropoietin production that stimulates osteoclast precursors and induces bone loss
- Iron deficiency - impacts procollagen hydroxylation and vit D metabolism

MGUS AND MM ARE NOT SO RARE

- **53.8%** of patients with MGUS were osteopenic and **26.2%** had osteoporosis
- Fracture risk in these patients does not depend on the immunoglobulin class of MGUS nor on the concentration of paraprotein = **all patients with MGUS have an increased risk of fracture**

*Pepe, J.; Petrucci, M.T.; Nofroni, I.; Fassino, V.; Diacinti, D.; Romagnoli, E.; Minisola, S. Lumbar bone mineral density as the major factor determining increased prevalence of vertebral fractures in monoclonal gammopathy of undetermined significance. Br. J. Haematol. **2006**, 134, 485–490.*

CASE # 2

- 50Y old M, healthy
- Back pain - fell off bike ~ 20 mi/h
- X-ray: L4 VCFx
- PmHx: R bimalleolar fracture- playing kickball

| | BMD (g/cm2) | T-score |
|-------|-------------|---------|
| LI-L3 | 0.859 | - 1.9 |
| LFN | 0.716 | - 1.6 |
| LTH | 0.834 | - 1.3 |
| RFN | 0.667 | - 1.9 |
| RTH | 0.810 | - 1.5 |

LABORATORY W/UP

- CMP normal except **TAP = 38 (39-117)**
- **BSAP = 4.6 (7.5-26.1)**
- Phos 4.5; PTH 24, Ca 9.3, alb 4.3
- **25OHD = 28.5 (30-100)**
- 24h UR Ca= 180 mg,
Vitamin B6 = 61.9 (5.3-46.7)

RESULT: POSITIVE



One Pathogenic variant identified in ALPL. ALPL is associated with autosomal dominant and recessive hypophosphatasia.

| GENE | VARIANT | ZYGOSITY | VARIANT CLASSIFICATION |
|------|-------------------------|--------------|------------------------|
| ALPL | c.1001G>A (p.Gly334Asp) | heterozygous | PATHOGENIC |

About this test

This diagnostic test evaluates 13 gene(s) for variants (genetic changes) that are associated with genetic disorders. Diagnostic genetic testing, when combined with family history and other medical results, may provide information to clarify individual risk, support a clinical diagnosis, and assist with the development of a personalized treatment and management strategy.

Hypophosphatasia in Adults: Clinical Assessment and Treatment Considerations

Jay R Shapiro ¹ and E Michael Lewiecki ²

¹Uniformed Services University of the Health Sciences, Bethesda, MD, USA

²New Mexico Clinical Research and Osteoporosis Center, Albuquerque, NM, USA

PAY ATTENTION TO TAP < 50 IN
ADULTS (OVER AGE 18)

FOR CHILDREN LOOK FOR **AGE-
APPROPRIATE** TAP

- Mutations involving the gene ALPL on chromosome 1 (encodes for tissue nonspecific alkaline phosphatase, TNSALP), an enzyme found on the outer surface of osteoblasts
- The accumulation of PPi (inorganic pyrophosphate - inhibitor of bone mineralization produced by osteoblasts and chondrocytes when TNSALP is deficient) impairs tissue calcium/phosphate formation of hydroxyapatite, leading to accumulation of **unmineralized osteoid**

HYPOPHOSPHATASIA IS A NOT SO RARE IN ADULT PATIENTS WITH FRACTURES



- Clinical presentation of HPP in adults is highly variable and depends on the residual level of enzymatic activity and the age at symptom onset
- The disease may be overlooked in childhood and only diagnosed during adulthood.
- It is important to recognize the disease to provide the better treatment of the fractures which are frequently complicated and associated with pseudarthrosis.
- Sometimes fibromyalgia and achy joints can be red flags from history
- Fractures, joint complications of chondrocalcinosis, calcifying polyarthrititis and multiple pains may reveal minor forms of the disease in adults.

Briot K, Roux C. Adult hypophosphatasia. Arch Pediatr. 2017;24(5S2):5S71-5S73.

IT IS OF MAJOR IMPORTANCE TO **PREVENT THE USE OF ANTI-RESORPTION DRUGS** FREQUENTLY PRESCRIBED FOR THE FRACTURES RELATED TO BONE FRAGILITY **WRONGLY ATTRIBUTED TO OSTEOPOROSIS IN THESE PATIENTS.**

- Bisphosphonates and possibly denosumab - lowers serum ALP, which is already low in patients with HPP and worsens osteomalacia
- Excessive vitamin D/calcium intake may aggravate the occurrence of hypercalcemia and hypercalciuria

DIAGNOSIS OF HPP

- Repeat total alkaline phosphatase
- Eliminate other causes

OTHER CAUSES OF LOW ALK PHOS

- Drugs: glucocorticoids, fibrates, estrogen, chemotherapy
- Zinc, Mg, vit C deficiency
- Vitamin D intoxication
- celiac disease
- Malnutrition/starvation
- multiple myeloma
- Hypothyroidism
- Hypoparathyroidism
- Cushing disease
- Milk-alkali syndrome
- Cardiac bypass syndrome
- Cleidocranial dysostosis
- Achondroplasia
- Radioactive heavy metals
- Pernicious anemia
- Profound anemia
- Wilson disease (hemolytic anemia)
- Improper blood collection (oxalate, EDTA)
- Blood transfusions
- Osteogenesis imperfecta type II

DIAGNOSIS OF HPP

- Repeat total alkaline phosphatase
- Eliminate other causes
- Fasting vitamin B6 (pyridoxal-5'-phosphate)
- Elevated 24h urine urinary of phosphoethanolamine (PEA)
- Genetic test - mutation in ALPL gene

CASE # 3

- 72 y old PMF
- PMHx: HTN, postsurgical hypothyroidism on replacement
- SHx neg

| | BMD (g/cm ²) | T-score |
|---------------|--------------------------|---------|
| LS | N/A (scoliosis) | N/A |
| LFN | 0.736 | - 2.2 |
| LTH | 0.802 | - 1.6 |
| RFN | 0.789 | - 1.8 |
| RTH | 0.849 | - 1.3 |
| I/3 L rad 33% | 0.523 | - 4.0 |

- **sCa = 10.5**, creat = 0.92 (eGFR 63)
- **PTH 76 (15-65)**
- 25OH vit D = 44
- **24h UR Ca = 235 mg**, creat 924 mg
- BSAP 15
- CTX 708
- US kidney - negative for KS

JAMA Surgery | Review

Indications for Surgical Management of Hyperparathyroidism A Review

Antonia E. Stephen, MD; Michael Mannstadt, MD; Richard A. Hodin, MD

[J Clin Endocrinol Metab.](#) 2014 Oct; 99(10): 3561–3569.

Published online 2014 Aug 27. doi: [10.1210/jc.2014-1413](#)

Consensus Statement

PMCID: PMC5393490

PMID: [25162665](#)

Guidelines for the Management of Asymptomatic Primary Hyperparathyroidism: Summary Statement from the Fourth International Workshop

[John P. Bilezikian](#), [Maria Luisa Brandi](#), [Richard Eastell](#), [Shonni J. Silverberg](#), [Robert Udelsman](#), [Claudio Marcocci](#),
[and others](#)

- An increase in serum calcium >1 mg/dL above the upper limit of normal.
- A reduction in BMD that is significantly decreased over the baseline measurement and a T-score that falls below -2.5 (any site).
- The occurrence of a fragility fracture or VCF on Xray, CT, MRI, VFA.
- The occurrence of a kidney stone (clinical or on imaging)
- A reduction in creatinine clearance to <60 mL/min.
- Age < 50 y old

MEDICAL MANAGEMENT HPTH

- Long-term observational studies indicate that **biochemistries and BMD remain stable for many years** in those followed non-operatively
- 15-year data suggest that **BMD starts to decline at cortical sites after 10 years of observation**
- 40% of patients developed one or more indications for parathyroidectomy over 15 years of follow-up
- Regular monitoring of biochemistries and of BMD with DXA is recommended for those who choose to be observed

Silverberg SJ, Shane E, Jacobs TP, Siris E, Bilezikian JP. A 10-year prospective study of primary hyperparathyroidism with or without parathyroid surgery *N. Engl. J. Med.* 1999; 341:1249–1255

Cope O. The study of hyperparathyroidism at the Massachusetts General Hospital *N. Engl. J. Med.* 1966; 274:1174–1182.

Yeh MW. Incidence and prevalence of primary hyperparathyroidism in a racially mixed population *J. Clin. Endocrinol. Metab.* 2013; 98:1122–1129.

Wermers RA. Incidence of primary hyperparathyroidism in Rochester, Minnesota, 1993–2001: an update on the changing epidemiology of the disease *J. Bone Miner. Res.* 2006; 21:171–177.

LOW BONE DENSITY - BISPHOSPHONATES

- Alendronate, improves the lumbar spine BMD without any changes in the serum calcium
- Alendronate has been shown to increase BMD in NPHPT
- Very few data are available for other bisphosphonates in PHPT
- Anti-resorptives can be considered in patients not undergoing parathyroidectomy who have osteoporosis, a history of fragility fracture or high fracture risk, though none are specifically approved for the treatment of PHPT.

Bilezikian JP. Primary Hyperparathyroidism. J Clin Endocrinol Metab. 2018;103(11):3993-4004.

HYPERCALCEMIA - CINACALCET

- Type 2 calcimimetic that binds to the CASR and increases its sensitivity.
- Reduces serum levels of calcium in patients with PHPT.
- Approved for PHPT by the European Medicines Agency in 2008 and by the FDA in 2011 for the treatment of severe hypercalcemia in patients with PHPT who are unable to undergo parathyroidectomy
- Maintains long-term normocalcemia across a wide spectrum of disease severity
- Neither BMD nor urinary calcium excretion improves with cinacalcet treatment,
- No data regarding reduction in the risk of nephrolithiasis

WHEN SHOULD REFERRAL TO AN ENDOCRINOLOGIST OR METABOLIC BONE SPECIALIST BE CONSIDERED?

- normal BMD and fracture without major trauma
- recurrent fractures or continued bone loss while receiving therapy without obvious treatable causes of bone loss
- less common secondary conditions (e.g., hyperthyroidism, hyperparathyroidism, hypercalciuria, or elevated prolactin),
- unexpectedly severe osteoporosis or unusual features such as young age or abnormal laboratory testing (e.g., low phosphorus, high or low alkaline phosphatase)
- artifacts on DXA that are unexplained,
- conditions that complicates management (e.g., decreased kidney function, hyperparathyroidism, or malabsorption).

SUMMARY

- Secondary causes for fragility fractures may be asymptomatic and require laboratory testing for detection.
- Because of the high prevalence of causes of secondary osteoporosis even in apparently healthy, postmenopausal women, laboratory testing should be considered for all women with osteoporosis.
 - Gallagher JC, Sai AJ Bone: is screening for secondary causes of osteoporosis worthwhile? *Nat. Rev. Endocrinol.* 2010;6:360-362. [EL 4; NE]
- This is reasonable, as a few simple laboratory tests provided useful information in 40 to 85% of women who did not have clinical evidence

Barzel US Recommended testing in patients with low bone density. *J. Clin. Endocrinol. Metab.* 2003;88:1404-1405; author reply 1405. [EL 2; ES]

Tannenbaum C, Clark J, Schwartzman K et al. Yield of laboratory testing to identify secondary contributors to osteoporosis in otherwise healthy women. *J. Clin. Endocrinol. Metab.* 2002;87:4431-4437. [EL 2; CSS]

Edwards BJ, Bunta AD, Simonelli C, Bolander M, Fitzpatrick LA. Prior fractures are common in patients with subsequent hip fractures. *Clin Orthop Relat Res.* 2007;461:226-230. [EL 3; ECON]

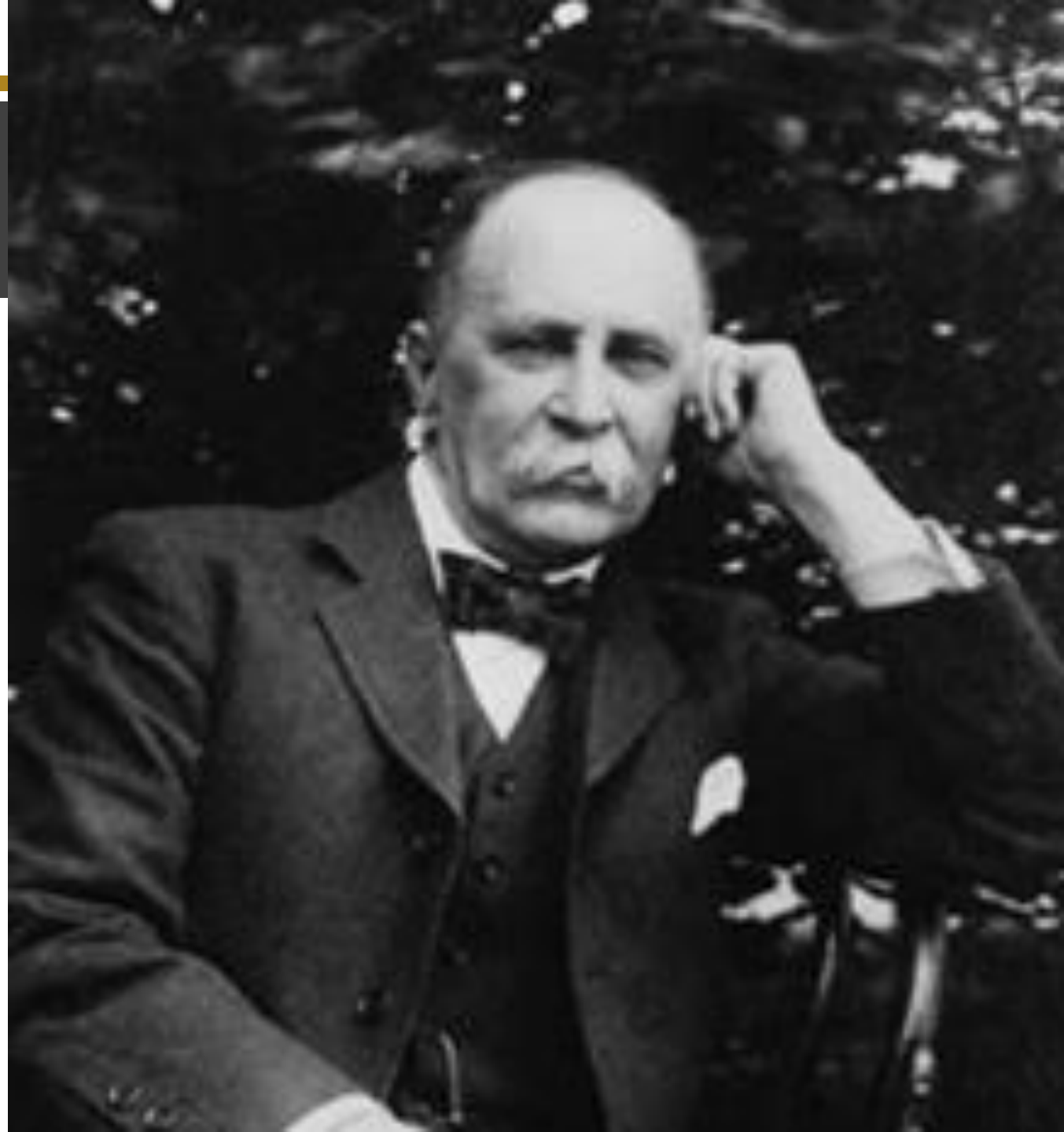
Camacho PM, Dayal AS, Diaz JL. Prevalence of secondary causes of bone loss among breast cancer patients with osteopenia and osteoporosis. *J Clin Oncol.* 2008;26:5380-5385. [EL 2; RCCS]

Lane NE. An update on glucocorticoid-induced osteoporosis. *Rheum Dis Clin North Am.* 2001;27:235-253. [EL 4; NE]

TREAT THE PERSON, NOT JUST THEIR BONES

*“The good physician treats the disease;
the great physician treats the patient who has the disease.”*

Sir William Osler



THANK YOU!

