Geriatric Endocrinology Pearls for the PALTC Practitioner

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1

Speaker Disclosures

The following speakers have disclosures:

- Naushira Pandya, M.D., CMD, FACP: no relevant financial relationships.
- Meenakshi Patel, MD, FACP, MMM, CMD: MD Multiple companies doing research and as a speaker but nothing relevant to this topic
- Elizabeth Hames, DO, CMD: employee of United Health Group

All financial relationships have been identified, reviewed, and mitigated by The Society prior to this presentation.

2

2

Learning Objectives

By the end of the presentation, participants will be able to:

- Employ treatment recommendations from current guidelines for management of osteoporosis
- Differentiate between primary and secondary hypothyroidism, and determine the management of hyperparathyroidism
- Identify clinical or laboratory findings indicating adrenal dysfunction, and initiate a preliminary evaluation
- Recognize that patients with refractory gastrointestinal symptoms may have an underlying endocrine disorder

3

3

Osteoporosis Treatment Updates for the PALTC Practitioner

Elizabeth Hames, DO, CMD

4

4

Definitions: Postmenopausal osteoporosis

estrogen deficiency causes increased osteoclast differentiation and activation → accelerated bone resorption and rapid bone loss → low bone mineral density and decreased bone strength

Increased risk of fragility fractures ***US: 50% of post-menopausal women*** ← In the US, 30% of women ≥65 yrs and 70-85% of PALTC residents have osteoporosis ← *1- Walker MD, and Shane E. Postmenopausal Osteoporosis. N Engl J Med 2023; 389:1979.*

5

5

BONE HEALTH SURVEY 2023

Women ≥60 years : over 7000 surveys

Brazil, Japan, Spain, South Korea, UK

43% had fracture following a minor fall or bump

33% did not have a diagnostic scan

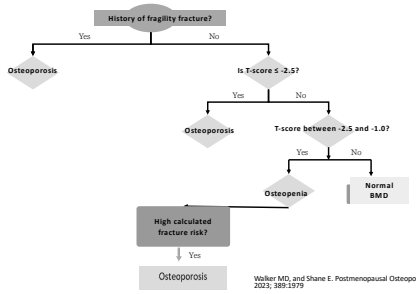
45% did not receive treatment for osteoporosis after fracture

31% stated that they had never discussed bone health or osteoporosis with their doctors

https://www.osteoporosis.foundation/wod2023-survey

6

Diagnosis of Osteoporosis



Walker MD, and Shane E. Postmenopausal Osteoporosis. N Engl J Med 2023; 389:1979

8

Treatment of Osteoporosis - Primary and Secondary Prevention

RISK FACTORS FOR OSTEOPOROSIS & FRACTURE

age
low weight
previous adult fracture
> 3 months glucocorticoid use
current tobacco / alcohol use
RA, osteomalacia, celiac dz
medications causing bone loss

- Lifestyle Modifications
  - all post-menopausal patients
- Pharmacologic Therapy
  - patients with high fracture risk

9

Treatment of Osteoporosis: Lifestyle Modifications

Weight-bearing exercise 30 minutes most days and fall prevention

Smoking cessation

Reduced alcohol consumption

Calcium: 1000 - 1200 mg/day

Vitamin D 400-1000 IU daily

8- Brooke-Wavell K, Skelton DA, Barker KL, et al. Strong, steady and straight: UK consensus statement on physical activity and exercise for osteoporosis. Br J Sports Med 2022.

9- Qaseem A, Hicks LA, Etxeandia-Ikobaltzeta I, et al. Pharmacologic treatment of primary osteoporosis or low bone mass to prevent fractures in adults: a living clinical guideline from the American College of Physicians. Ann Intern Med 2023; 176:224-38.

10 - Camacho PM, Petak SM, Binkley N, et al. American Association of Clinical Endocrinologists/American College of Endocrinology clinical practice guidelines for the diagnosis and treatment of postmenopausal osteoporosis — 2020 update:executive summary. Endocr Pract 2020;26:564-70

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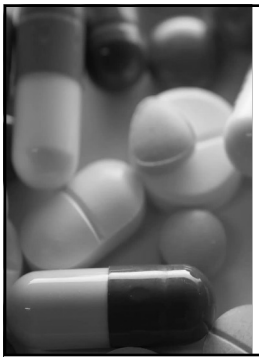

Osteoporosis Pharmacotherapy

Consider:

Severity of osteoporosis

Risk of fracture

Calculate FRAX score – important!

Co-morbidities

Patient factors and preference

11

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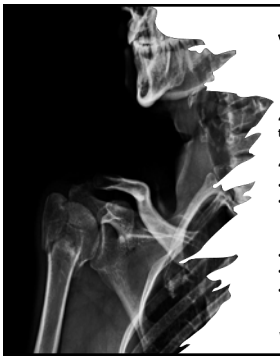

Very High Fracture Risk

"High fracture risk" : meeting minimal intervention thresholds (which vary by guideline)

"Very high fracture risk":

- **No consensus definition – criteria vary**
- **May influence the choice of initial medication**

- **T-score of <-2.5 plus spine or hip fracture**
- **T-score of < -3.0 without fragility fracture**
- **History of multiple spine or hip fractures**

Walker MD, Shane E. Postmenopausal Osteoporosis. N Engl J Med 2023; 389:1979.

12

12

Pharmacotherapy – when to begin

GUIDELINE	THRESHOLD FOR TREATMENT WITH HIGH FRACTURE RISK
AACE – ACE 2020	• T-SCORE ≤-2.5 AT SPINE, FEM NECK, OR TOTAL HIP **OR** • OSTEOPENIA (T-SCORE -1.0 TO -2.49) + HX FRAGILITY FRACTURE OF HIP OR SPINE + FRAX HIGH PROB OF FRACTURE
AMERICAN COLLEGE OF PHYSICIANS (ACP) 2023	• T-SCORE ≤-2.5 • INDIVIDUALIZE IN PERSONS >65 WITH OSTEOPENIA
BONE HEALTH AND OSTEOPOROSIS FOUNDATION	• T-SCORE ≤-2.5 AT SPINE, FEM NECK, OR TOTAL HIP OR • HIP OR VERTEBRAL FRACTURE WITH ANY BMD OR • OSTEOPENIA & FRAX MAJOR FRACTURE RISK ≥ 20% OR HIP FRACTURE RISK ≥ 3% OR • OSTEOPENIA WITH FRACTURE OF PROX HUMERUS, PELVIS, OR DISTAL FOREARM**
ENDOCRINE SOCIETY 2019-2020	• POSTMENOPAUSAL WOMEN WITH HIGH FRACTURE RISK, ESPECIALLY IF HISTORY OF RECENT FRACTURE
ESCEO and IOF	• WOMEN > 65 YRS WITH PREVIOUS FRAGILITY FRACTURE **OR** • WOMEN > 65 YRS WITHOUT FRACTURE HX BUT WITH A FRACTURE RISK EQUAL TO WOMEN WITH FRACTURE HX

1- Walker MD, Shane E. Postmenopausal Osteoporosis. N Engl J Med 2023; 389:1979.
2- Qaseem A, Hicks LA, Etxeandia-Ikobaltzeta I, et al. Pharmacologic treatment of primary osteoporosis or low bone mass to prevent fractures in adults: a living clinical guideline from the American College of Physicians. Ann Intern Med 2023; 176:224-38.

13

13

Treatment of Osteoporosis: Pharmacotherapy

Antiresorptives – reduce vertebral, non-vertebral*, and hip fractures*

Bisphosphonates – bind to hydroxyapatite and inhibit resorption; Avoid with Cr Cl < 30-35, hypocalcemia, or esophageal dysmotility/varices. GI irritation. Atypical femoral fracture and jaw osteonecrosis rare.

RANK ligand inhibitor (denosumab) – binds to RANKl and inhibits formation and survival of osteoclasts. Avoid in hypocalcemia and avoid abrupt cessation, risk of rebound bone loss and fracture. Atypical femoral fracture and jaw osteonecrosis rare.

Estrogens (CEE) – decrease osteoclast resorption. Avoid with history of VTE, CVA/TIA, history or increased risk breast or endometrial cancer

SERMs -selective estrogen receptor modulators (raloxifene or bazedoxifene + CEE) – decreases osteoclast activity. Avoid with history of VTE, PE, retinal vein thrombosis

* Ibandronate, raloxifene, and bazedoxifene + CEE not shown to reduce hip or non-vertebral fractures

Walker MD, Shane E. Postmenopausal Osteoporosis. N Engl J Med 2023; 389:1979.

14

14

Treatment of Osteoporosis: Pharmacotherapy

Anabolic agents - reduce vertebral and non-vertebral fractures

PTH receptor agonists – increase bone formation. Not shown to reduce hip fractures.

- teriparatide (PTH analogue)
- abaloparatide (PTHrP analogue)
- avoid in history of or high risk of bone malignancy, Paget's disease, and hypercalcemia

Anabolic-antiresorptive - reduce vertebral, non-vertebral, and hip fractures

Sclerostin inhibitor (romosozumab) – monoclonal antibody against sclerostin. Increases bone formation and decreases bone resorption. Avoid if recent stroke, MI, high CV risk, hypocalcemia.

- Hip and non-vertebral fracture reduction only as compared to alendronate, not compared to placebo.

Walker MD, Shane E. Postmenopausal Osteoporosis. N Engl J Med 2023; 389:1979.

15

15

BISPHOSPHONATES

alendronate, risedronate, ibandronate, zoledronic acid

- Most guidelines recommend bisphosphonates as initial treatment of post-menopausal OP in patients with **high fracture risk**
- (AACE/ACE/Bone Health OP Foundation/Endocrine Society) : Treat for 5 yrs, consider drug holiday, continue another 5 yrs or consider alternate agent if fracture risk has remained high
- (AACE/ACE/Endocrine Society) zoledronic acid: consider drug holiday after 3 yrs
- ACP (2023) - treatment for >3 to 5 years only for reduction of vertebral fractures, consider stopping after 5 yrs unless strong reason to continue
- ESCEO and IOF - review need for treatment after 3-5 years

- **MOST GUIDELINES RECOMMEND REPEATING DEXA EVERY 1-2 YEARS**

1 - Walker MD, Shane E. Postmenopausal Osteoporosis. N Engl J Med 2023; 389:1979.

2- Qaseem A, Hicks LA, Etxeandia-Ikobaltzeta I, et al. Pharmacologic treatment of primary osteoporosis or low bone mass to prevent fractures in adults: a living clinical guideline from the American College of Physicians. Ann Intern Med 2023; 176:224–38.

3 - Camacho PM, Petak SM, Binkley N, et al. American Association of Clinical Endocrinologists/American College of Endocrinology clinical practice guidelines for the diagnosis and treatment of postmenopausal osteoporosis – 2020 update. Endocr Pract 2020; 26:1–46.

Kanis JA, Cooper C, Rizzoli R, Reginster J-Y. European guidance for the diagnosis and management of osteoporosis in postmenopausal women. Osteoporos Int 2019;30:3–44.

Shoback D, Rosen CJ, Black DM, Cheung AM, Murad MH, Eastell R. Pharmacological management of osteoporosis in postmenopausal women: an endocrine society guideline update. J Clin Endocrinol Metab 2020;105:587–94.

16

16

RANK ligand inhibitor (denosumab)

- Higher absolute increases of BMD than bisphosphonates, limited evidence for more fracture reduction[14]
- Second-line therapy for women who are not able to take bisphosphonates (ACP 2023). Debated for use as initial therapy
- Need consistent dosing every 6 months, > 4-month dose delay = 4X increased vertebral fracture rate [15]
- Overall duration uncertain – reassess fracture risk 5-10 yrs (multiple guidelines)
  drug holiday not recommended (AACE/ACE/Endocrine Society)
- Concern for rebound bone loss and increase in vertebral fractures with abrupt discontinuation

Freemantle N, Satram-Hoang S, Tang ET, et al. Final results of the DAPS (Denosumab Adherence Preference Satisfaction) study: a 24-month, randomized, crossover comparison with alendronate in postmenopausal women. Osteoporos Int 2012; 23:317-26.
Lyu H, Yoshida K, Zhao SS, et al. Delayed denosumab injections and fracture risk among patients with osteoporosis: a population-based cohort study. Ann Intern Med 2020;173:616-26.

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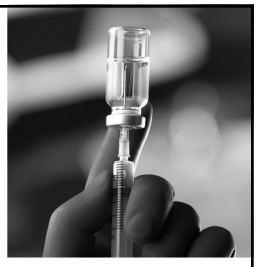
17

PTH receptor agonists (teriparatide & abaloparatide)



- Treatment for 18-24 months reduced vertebral & non-vertebral fracture risk (not hip fractures)
- Limited data for greater BMD in spine than alendronate[1]
- Decreases vertebral fractures more than risendronate[1]
- Most guidelines recommend for only for patients with:
  - very high fracture risk
  - no response to other agents
  - intolerance of all other agents
- Must be followed by antiresorptive therapy after completion[1]

Walker MD, Shane E. Postmenopausal Osteoporosis. N Engl J Med 2023; 389:1979.

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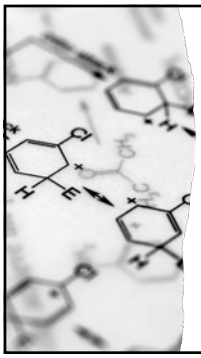

Sclerostin inhibitor – romosozumab

- **Anabolic-antiresorptive agent**
- **Several guidelines recommend as initial agent only if very high fracture risk, treatment for 1 year (AACE/ACE/Endocrine Society)**
- **Increased BMD more than teriparatide in phase 2 study**
- **Reduced vertebral and non-vertebral fractures compared to placebo (FRAME trial)[16]**
- **Need to continue with bisphosphonate or denosumab after completion of romosozumab**
- **Black-box warning to avoid within 1 year of MI or stroke**

Walker MD, Shane E. Postmenopausal Osteoporosis. N Engl J Med 2023; 389:1979.

Cosman F, Crittenden DB, Adachi JD, et al. Romosozumab treatment in postmenopausal women with osteoporosis. N Engl J Med 2016;375:1532-43.

19

19

Treatment approach: very high fracture risk

GUIDELINE	INITIAL TREATMENT FOR VERY HIGH RISK OF FRACTURE
AACE/ACE 2020	abaloparatide or teriparatide for 2 yrs, then antiresorptive OR romosozumab for 1 yr, then antiresorptive OR treat with alendronate or risendronate for 6-10 yrs or zoledronic acid for 6 years before possible holiday
ACP 2023	teriparatide OR romosozumab, then antiresorptive
Endocrine Society and Bone Health / Osteoporosis Foundation	teriparatide OR abaloparatide if not high cardiovascular risk
ESCEO and International OP Foundation	teriparatide is preferred agent

1 - Walker MD, Shane E. Postmenopausal Osteoporosis. N Engl J Med 2023; 389:1979.

20

20

ACP 2023 Osteoporosis Guideline

bisphosphonates for initial pharmacologic treatment to reduce the risk of fractures in postmenopausal females with primary osteoporosis
(strong evidence)

bisphosphonates for initial pharmacologic treatment to reduce the risk of fractures in males with primary osteoporosis
(low evidence)

denosumab – second-line pharmacologic treatment to reduce risk of fractures in postmenopausal females with primary osteoporosis who cannot take bisphosphonates
(moderate evidence)

romosozumab, (moderate evidence) or **teriparatide**, (low evidence), followed by a bisphosphonate, to reduce risk of fractures in females with primary osteoporosis with very high risk of fracture

individualized approach regarding whether to start pharmacologic treatment with a bisphosphonate in females over the age of 65 with osteopenia to reduce the risk of fractures (low evidence)

9- Qaseem A, Hicks LA, Etxeandia-Ikobaltzeta I, et al. Pharmacologic treatment of primary osteoporosis or low bone mass to prevent fractures in adults: a living clinical guideline from the American College of Physicians. Ann Intern Med 2023; 176:224-38.

21

21

Controversies regarding treatment of osteoporosis in PALTC setting

- 3 guidelines address PALTC AMDA 2009, Australian 2021, Canadian 2015:
  - individualized fall / fracture risk assessment
  - Calcium (max 1500 mg daily) and vitamin D (800-2000 daily)
  - Consider anabolic therapy if fracture after ≥ 1 year of antiresorptive use and T score < - 3 or 2 + fractures
- Inconsistent use of pharmacologic therapies in PALTC for fracture prevention: 40% to 1.5%
- Considerations: estimated benefit of treatment, life expectancy, fall risk, goals of care and preferences, polypharmacy, co-morbidities
- Consider de-prescribing or to not begin medication if life expectancy < 2 years, decreasing mobility with decreasing fall risk, increasing treatment burden, and/or goal is comfort care
- Recommendation for screening with a frailty tool, fall prevention strategies, individualized approach to treatment
- Routine BMD testing not recommended
- Special consideration for patients being considered for discontinuation of denosumab who have remaining fall risk – possible continuation of one year bisphosphonate

J.D. Niznik et al. Controversies in Osteoporosis Treatment of Nursing Home Residents. JAMDA 23 (2022).

22

22

Clinical Case

Mrs. Jones is an 83-year-old female being admitted to an ALF:

- She has a past medical history of an acute ischemic left MCA stroke 3 months ago, AFib, osteoporosis, type 2 DM, and HTN.
- She has no fracture history.
- Her last DEXA was 2 years ago, T-score -2.85 in the femoral neck
- She was taking an oral bisphosphonate at the time of her stroke with no adverse effects, it was stopped when she was hospitalized.
- She has no residual dysphagia after the stroke, ambulates more than 200 feet with a rolling walker, and her cognition is good.

23

23

Clinical Case

What is Mrs. Jones' risk for fracture?

A – low risk
B – moderate risk
C – high risk
D – very high risk

Which of the following would be recommended?

A – no pharmacotherapy
B – oral alendronate
C – romosozumab
D - teriparatide

24

24

Take Home Messages

- Osteoporosis can be diagnosed by history of fragility fracture, BMD, and/or calculated 10-yr risk of fracture (FRAX).
- Bisphosphonates are a mainstay of initial treatment to reduce the risk of fractures in postmenopausal females with primary osteoporosis.
- The RANK ligand inhibitor, denosumab, is second line therapy for patients who are unable to take bisphosphonates.
- Discontinuation of denosumab causes rebound bone loss, and indefinite treatment with denosumab or transition to bisphosphonates after discontinuing denosumab is recommended.
- Anabolic (teriparatide) and anabolic-antiresorptive (romosozumab) agents may be used as short-term initial therapy for post-menopausal osteoporosis in patients with very high risk of fracture and should be followed by antiresorptive agents.
- When making decisions about pharmacotherapy for osteoporosis in PALTC, consider severity of osteoporosis, risk of fracture, co-morbidities, lag time to benefit, and patient factors and preferences.

25

25

THANK YOU!

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26

26

Hypothyroidism and Hyperparathyroidism

Meenakshi Patel, MD, MMM, CMD
Clinical Assoc. Prof., Wright State University
Boonshoft School of Medicine, Dayton OH

27

Learning Objectives

At the conclusion of this session, learners will be able to:

1. Employ treatment recommendations from the updated 2021 osteoporosis guidelines

2. Differentiate between primary and secondary hypothyroidism, and determine the management of hyperparathyroidism

3. Identify clinical or laboratory findings indicating adrenal dysfunction, and initiate a preliminary evaluation

4. Recognize that patients with refractory gastrointestinal symptoms, may have an underlying endocrine disorder

28

Objectives for this section

- Interpretation of thyroid function tests
- Management of hypothyroidism-differentiating primary and secondary
- Sub-clinical thyroid disease and when to treat
- Management of hyperparathyroidism

29

Age-associated changes in the thyroid

- Progressive fibrosis and atrophy
- Hypothalamic-pituitary-thyroid (HPT) axis remains intact.
- Decline in TSH, reduced thyroxine (T4) and triiodothyronine (T3) secretion
- Due to reduced clearance, T4 levels remain normal
- T3 declines in advanced old age, and the inactive metabolite reverse T3 (rT3) increases
- Acute or chronic illness may lead to abnormalities of thyroid function as can several medications

Ajish. Indian J Endo and Metab 2012(16)4, Mitro. Maturitas 2100;70:5

30

Causes of hypothyroidism in the elderly

Primary hypothyroidism

- Chronic autoimmune hypothyroidism (Hashimoto's thyroiditis)
- Post ^{131}I treatment for hyperthyroidism
- Subtotal or total thyroidectomy
- Radiation therapy for head and neck cancer
- Drugs

Central (secondary)hypothyroidism <1%

- Hypothalamic tumors or infiltrative lesions
- Pituitary tumors or infiltrative lesions
- Pituitary surgery
- Head injury or surgery
- Cranial radiation
- Stroke, hemorrhage or ischemia

Gibbons V, Lawrenson, et al. NZMJ 2012;125:83-90.

31

Drugs affecting thyroid function

Effect	Drugs
May cause hypothyroidism	Lithium, iodine (in kelp, contrast media, topical iodine), amiodarone, interferon alpha)
May cause hyperthyroidism	Amiodarone, iodine, interleukin-2, interferon alpha
Reduce conversion of T4 to T3	Glucocorticoids, iodine, propylthiouracil, propranolol, amiodarone
Suppress TSH	Dopamine, dobutamine, glucocorticoids, phenytoin, bromocriptine, somatostatin analogues, metformin, mitotane
Increase clearance of T4	Carbamazepine, phenytoin, rifampin, phenobarbital
Reduce binding of T4 to thyroid-binding globulin	Phenytoin, carbamazepine, salsalate, NSAIDS, furosemide, heparin

Ajish. Indian J Endo and Metab 2012(16)4; HB Burch. N Engl J Med 2019; 381.

32

Symptoms and Signs of Hypothyroidism in Older Adults

SYMPTOMS
- Fatigue 68%
- Cold intolerance
- Constipation, ileus
- Dysphagia
- Exertional dyspnea, atypical CP
- Lack of concentration
- Memory loss, delusions or psychosis
- Hearing loss
- Depression
- Generalized weakness or muscle cramps 53%

SIGNS
- Alopecia
- Xerosis
- Hoarseness
- Weight gain
- Bradycardia, diastolic HTN
- Worsened congestive heart failure
- Anemia
- Hyperlipidemia, elevated CPK
- Myxedema, macroglossia
- Neuropathy, slowed reflexes
- Confusion, withdrawal, psychosis

33

Interpretation of Thyroid Function Tests

	TSH	FT4	TT3	Tg	Anti-TG Ab
Subclinical hypothyroidism	↑	NL	NL		
Hypothyroidism	↑	↓	NL		
Central hypothyroidism	↓	↓	↓		
Subclinical hyperthyroidism	↓	NL	NL		
Hyperthyroidism	↓	↑	↑		
TSH-producing pituitary adenoma	↑	↑	↑		
Intermittent med adherence	↑ or NL	↑	↑		
Non-thyroidal illness	NL	↓	NL or ↓		
Thyroiditis/thyroid injury	NL or ↓	NL or ↑	NL or ↑	↑	NL or ↑
Persistent thyroid cancer	NL ↓ ↑	NL ↑ ↓		NL or ↑	NL or ↑

Pandya, N., & Hames, E. (2023). Thyroid Disorders in Older Adults. In Geriatric Medicine: A Person-Centered Evidence Based Approach (pp. 1-20). Cham: Springer International Publishing.

34

Treatment of hypothyroidism

- Goal: Normalize TSH, achieve a euthyroid state
- Synthetic thyroid hormone preparations preferred (rather than thyroid extracts) due to longer half-life and a more constant serum concentration
- Initial replacement dose usually 25-50 µg/day
- If significant cardiac co-morbidities, start on 12.5–25 µg/day and adjust dose by a similar amount every 3-6 weeks until the TSH has normalized and then follow every 6–12m
- **In primary hypothyroidism, the TSH alone can be used to monitor treatment**
- **In those with central (secondary) hypothyroidism, a free T4 level should be used**
- If no residual thyroid function exists, the daily replacement dose of levothyroxine is usually 1.6 µg/kg body weight (typically 100–150 µg).

ATA/AACE Guidelines, Nov 01, 2012

35

Cautions and caveats with thyroid replacement

- Dosage adjustments should take into account any worsening condition such as AF, HF or osteoporosis
- Avoid low normal or subnormal TSH levels.
  - Thyroxine can be held for days to weeks and restarted at a lower dose once the patient is stable
- **Linear changes in the concentration of T4 correspond to logarithmic changes in serum TSH**
  - If abrupt discontinuation or omission of levothyroxine therapy during a care transition, there may be a marked rise in the TSH level.
- **When resumed the dose of levothyroxine should be the prior documented dose and measurement of free T4 may be helpful**

ATA/AACE GUIDELINES| NOVEMBER 01, 2012

36

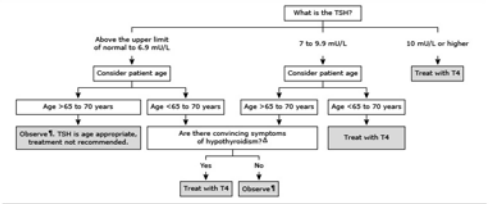
Subclinical hypothyroidism in >65 y olds

- TSH above ref range with serum free T4 within ref range (but upper limit of TSH is higher with age)
- Prevalence 10% in women and 4% in men >60
- Treat the whole patient and not the thyroid function tests
- Exclude other causes of high TSH (TSH hormone resistance, lab error, pituitary tumor, non-thyroidal illness, post partum thyroiditis)
- Treat if TSH is >10 in those >65 y
- Treat if TSH is 7.0-9.9 mU/L, and patient has convincing symptoms; goal NL TSH
- Observe if TSH is N-6.9 mU/L (TSH is age-appropriate); avoid treatment if >80y
- No cardiac, fatigue, or strength benefits in treating older adults with SCH

Razvii Arch Int Med 2012, TRUST Study NEJM 2017
Biondi B, Cappola A, Cooper D. Subclinical Hypothyroidism. *JAMA.* 2019;322(2)

37

Indications for thyroid hormone replacement in nonpregnant adults with subclinical hypothyroidism*



Free T4: free thyroxine; T4: levothyroxine; TSH: thyroid-stimulating hormone.
* Subclinical hypothyroidism is defined by a TSH above the normal reference range with a normal free T4, confirmed with repeat measurement.
¶ For patients not treated with T4, monitor TSH and free T4 initially at six months, and if stable, yearly thereafter.
Δ Convincing symptoms of hypothyroidism (new or worsening fatigue, constipation, cold intolerance) or growing goiter.

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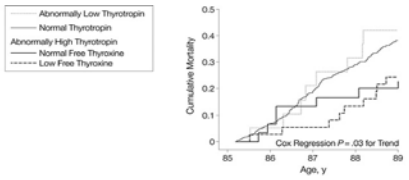
38

Cumulative Mortality of Participants Based on Clinical Stratification of Thyroid Status



Leiden 85 + study
N=558
4 yr follow-up

In the general population of the oldest old, elderly individuals with abnormally high levels of thyrotropin do not experience adverse effects and may have a prolonged life span

Gussekloo, J. et al. JAMA 2004;292:2591-2599.

39

Secondary hypothyroidism and its implications

- Secondary hypothyroidism may be associated with partial or complete HYPOPITUITARISM, and is difficult to diagnose in patients in PALTC patients as the presentation and symptoms are often missed or attributed to other chronic conditions or age.
- The prevalence of hypopituitarism in the elderly is unknown
- Non-specific clinical presentation (weight gain, fatigue, low muscle strength, hypotension, cold intolerance) depending on pituitary deficit
- Older patients with CV and PAD are prone to hypopituitarism due to a more fragile hypothalamic/pituitary circulation
- The etiology is varied although ASCVD risk factors were present in a majority is a case series
- Patients with traumatic brain injury should be monitored closely for hypopituitarism; often under recognized and symptoms may occur immediately post trauma, or after several months to years

Pandya, N., Sanders, D. L., & Makhijani, M. (2008).JAMDA, 9(3), B24.
Curtò, L., & Trimarchi, F. (2016). Hypopituitarism in the elderly: Journal of Endocrinological Investigation, 39, 1115-1124.

40

Take Home Messages

- Subclinical thyroid disease may be treated if criteria are met
- LTC practitioners need to have a high index of suspicion, if thyroid function tests suggest secondary hypothyroidism.
- It may indicate more extensive pituitary failure which could be treatable with thyroxine and glucocorticoids
- The diagnosis of partial or complete pituitary hypofunction can be made with readily available blood tests and neuroimaging

42

42

Hyperparathyroidism

43

43

Case:

- A 79-year old nursing home resident with hypertension, osteoporosis, type 2 diabetes, and a distant history of nephrolithiasis
- Recurrent complaints of malaise constipation and abdominal discomfort
- No response to scheduled doses of sorbitol and stool softeners. Medications include metformin 500 mg BID, valsartan/Hctz 160/25 mg daily, vitamin D 3000 IU daily.
- Her electrolytes are normal except for a repeat serum calcium of 10.9 mg/dL (8.6-10.3 mg/dL). She has normal thyroid function.

44

What is the next most appropriate step to find a cause of her hypercalcemia?

A. Measure an intact PTH level

B. Discontinue valsartan

C. Discontinue vitamin D since this can cause hypercalcemia.

D. Measure her calcium creatinine clearance

E. Measure serum protein electrophoresis

45

Hypercalcemia

- Can be a manifestation of a serious illness such as malignancy or detected coincidentally by lab testing in a patient with no obvious illness
- **Whenever hypercalcemia is confirmed, a definitive diagnosis must be established**
- Hyperparathyroidism is a chronic disorder in which manifestations, if any, may be expressed only after months or years
- Malignancy is the second most common cause of hypercalcemia in adults

46

Clinical Features are Helpful in Differential Diagnosis

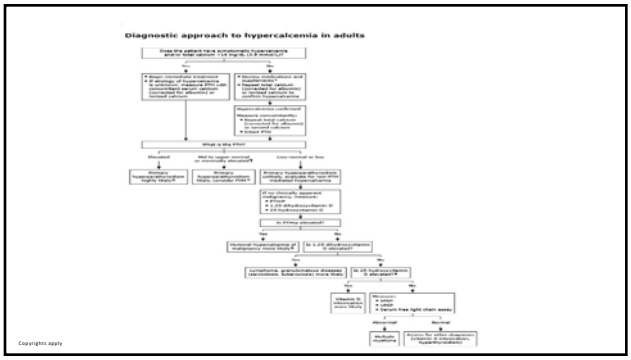
- **Symptoms; fatigue, depression, confusion, anorexia, vomiting, constipation, urinary frequency, short QT**
- Hypercalcemia in an asymptomatic adult is usually due to primary hyperparathyroidism (PHPT)
- FH of HPTH (Multiple Endocrine Neoplasia)
- In malignancy-associated hypercalcemia, symptoms of malignancy present
- Dietary history and use of vitamins or drugs
- ***Do not cut corners on the physical exam! (neck scars, nodes, breast, rectal, genital exam)***

47

Severity of Hypercalcemia and Clinical Manifestations

Calcium level	Clinical correlation
>2.9 to 3 mmol/L (11.5 to 12.0 mg/dL)	Neuropsychiatric, GI, renal symptoms
>3.2 mmol/L (13 mg/dL)	Calcification in kidneys, skin, vessels, lungs, heart, and stomach
3.7 to 4.5 mmol/L (15 to 18 mg/dL),	Medical emergency; coma and cardiac arrest

48



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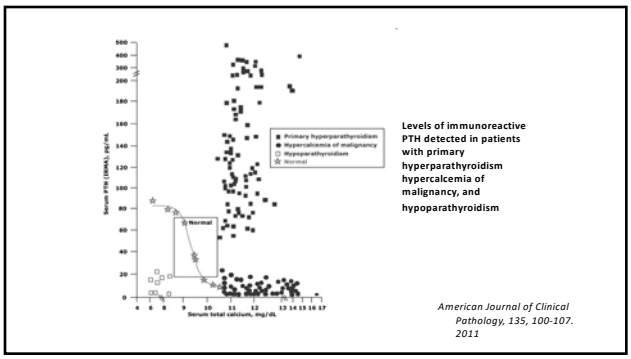

Levels of immunoreactive PTH detected in patients with primary hyperparathyroidism hypercalcemia of malignancy, and hypoparathyroidism

American Journal of Clinical Pathology, 135, 100-107. 2011

50

Hyperparathyroidism

- Primary–adenoma, hyperplasia or carcinoma
- Secondary–renal disease
- Tertiary– secondary hyperplasia leads to autonomous over activity of the parathyroid glands usually in renal failure

51

Primary hyperparathyroidism

- Hypercalcemia
- Hypercalciuria
- Hyperphosphaturia
- Kidney: Calcinosis, stone formation, recurrent infection and impaired renal function

52

Primary Hyperparathyroidism - Etiology

- **Prevalence:** 23 cases per 10,000 women and 8.5 per 10,000 men, estimated
- **Solitary Adenomas**
  - one or more hyperfunctioning glands
  - usually a benign adenoma and rarely a parathyroid carcinoma
  - In 15% of patients, all glands are hyperfunctioning
  - ***chief cell parathyroid hyperplasia*** is usually hereditary and frequently associated with other endocrine abnormalities

53

Causes of Primary Hyperparathyroidism

- Radiation exposure; head and neck 30 y prior, >1200 rads
- Radioactive iodine therapy (possibly)
- Hereditary syndromes with genetic or chromosomal defects
  - MEN 1 and MEN 2A (multiple tumors)
  - Hyperparathyroidism jaw tumor syndrome
- Vitamin D receptor gene (alters expression of adenoma)

54

Signs and Symptoms of Hyperparathyroidism

- Over half are asymptomatic
- Neuromuscular manifestations; weakness, fatigability, depression, anxiety, difficulty concentration
- Gastrointestinal manifestations are sometimes subtle
- Renal: nephrocalcinosis or recurrent nephrolithiasis (in <20%- ca oxalate or phosphate)
- Increased bone turnover (↑ bone sp Alk Phos, osteocalcin)
- ↓ cortical bone density (DXA hips or distal radius), spine relatively preserved
- HTN, changes in LV mass and function, increased mortality observed

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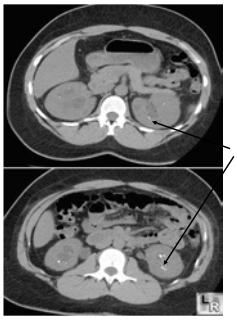
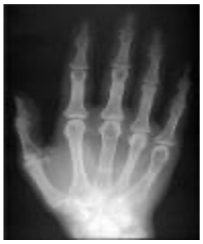


Primary hyperparathyroidism is single most common cause of nephrocalcinosis in adults

56

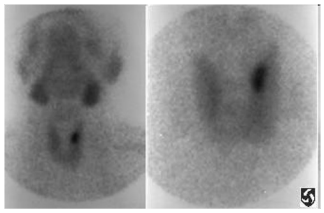
Radiological Findings in PHPT



In primary HPTH there is absorption of the tufts of the terminal phalanges in the hands and feet and subperiosteal bone resorption with particular effect at the level of the bone metaphysis.

57

Preoperative Functional Scan with 99mTc-sestamibi to Identify the Location of the Abnormal Gland



58

Guidelines for surgery in asymptomatic primary hyperparathyroidism (NIH consensus)

Measurement	Indication(s) for surgery
Serum calcium	>1 mg/dL (0.25 mmol/L) above the upper limit of normal
Skeletal	1. BMD by DXA: T-score ≤−2.5 at lumbar spine, total hip, femoral neck, or distal 1/3 radius[¶] 2. Vertebral fracture by radiograph, CT, MRI, or VFA
Kidney	1. eGFR <60 mL/min/1.73 m^2 2. 24-hour urine for calcium >250 mg/day (6.25 mmol/day) in women and >300 mg/day (7.5 mmol/day) in men 3. Presence of nephrolithiasis or nephrocalcinosis by radiograph, ultrasound, or CT
Age	<50 years

Patients need to meet only 1 of these criteria to be advised to have parathyroid surgery. They do not have to meet more than 1.

59

Surgical Treatment

- Parathyroid exploration requires an experienced surgeon- >97% cure in asymptomatic PHPT
- Conservative surgery is favored, i.e., minimally invasive
- Improved preoperative localization and intraoperative monitoring by PTH assays
- High resolution neck ultrasound AND
- Intraoperative sampling of PTH before and at 5-min intervals after removal of a suspected adenoma to confirm a rapid fall (>50%) to normal levels of PTH
- Multiple gland hyperplasia- totally remove three glands with partial excision of the fourth gland or sc. implantation of part of gland
- Older adults do well, but slightly longer hospital stays

Bilezikian, J. P., Silverberg et al, J. T. (2022). Journal of Bone and Mineral Research, 37(11), 2391-2403.
Young, V. N., Osborne, et al (2010). The Laryngoscope, 120(2), 247-252.

60

Treatment

- Adequate hydration
- Phosphate ingestion
- Adequate dietary calcium
- Parathyroidectomy: Indications
  - Marked and unremitting hypercalcemia
  - Recurrent renal calculi
  - Progressive nephrocalcinosis
  - Severe osteoporosis

61

Medical Management of Hyperparathyroidism (if surgery is not an option)

- Correct Ca and Vit D deficiency
  - calcium-sufficient diet (1000 to 1200/d) and maintain 25-OH D level 20-30 ng/m; with the use of vitamin D supplements
  - Oral hydration
- Bisphosphonates 5% increase in bone density in the spine with alendronate in asymptomatic hyperparathyroid patients (no change in PTH or Ca)
- Denosumab
- Calcimimetics, (cinacalcet 30 mg BID) decrease Ca levels by 1mg/dL and lower PTH levels by 19%; indicated for severe disease and parathyroid cancer
  - No significant effect on bone loss
- Thiazide diuretics- if urinary calcium is high and risk of nephrolithiasis

62

Secondary hyperparathyroidism; elevated PTH as a response to hypocalcaemia

- Seen in renal rickets and renal osteomalacia
- Treatment is directed at primary condition

63

THANK YOU!

64

Adrenal dysfunction in older adults

Naushira Pandya MD, CMD, FACP

65

Learning Objectives

At the conclusion of this session, learners will be able to:

1. Employ treatment recommendations from the updated 2021 osteoporosis guidelines

2. Differentiate between primary and secondary hypothyroidism, and determine the management of hyperparathyroidism

3. Identify clinical or laboratory findings indicating adrenal dysfunction, and initiate a preliminary evaluation

4. Recognize that patients with refractory gastrointestinal symptoms, may have an underlying endocrine disorder

66

Adrenal Insufficiency; Epidemiology

- Incidence 15.5/100,000 population in a Taiwan retrospective study, 80% >60 yrs
- Comorbidities: pneumonia and UTI, electrolyte abnormalities- pneumonia most common cause of hospitalization and death
- Retrospective 5-yr chart study of 3 extended care facilities in Hong Kong
  - 38% of 242 patients tested with synthetic ACTH, has AI, no difference in LOS and mortality
  - Infection and non-specific presentation noted again

Chen, Y. C., Chen, et al. (2010). The Tohoku Journal of Experimental Medicine, 221(4), 281-285.
Miu, D. K. Y., Man, S. P., & Tam, S. K. F. (2020). European Journal of Geriatrics & Gerontology, 2(3).

67

Acute Adrenal Insufficiency (AI)

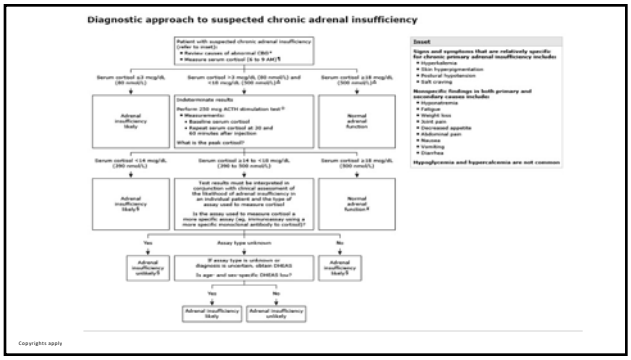
- **Causes of primary AI**: autoimmune disease, infection, tumor, hemorrhage
- **Secondary AI more common**: hypothalamic or pituitary disease
- Vague non-specific symptoms: anorexia, fatigue, fever, GI discomfort, hypoglycemia
- May progress to adrenal crisis with electrolyte disturbance, change in consciousness, or even shock, coma or death
- In adrenal crisis, generalized abdominal tenderness elicited on deep palpation; mechanism unclear; serositis?
- Signs and symptoms of bilateral adrenal hemorrhage include abdominal, flank, back, and lower chest pain, anorexia, nausea and vomiting, and abdominal rigidity
- May suggest a surgical cause, but the importance of a high level of clinical suspicion of adrenal crisis, and prompt management

68

Chronic adrenal insufficiency

- Signs and symptoms may be vague and non-specific leading to delay in diagnosis
- Nausea, persistent vomiting, and abdominal pain in 49–62%
- Constipation alternating with diarrhea; and weight loss of up to 2–15 kg noted in 66–76%, largely due to anorexia

69



70

Refractory gastrointestinal symptoms may have an endocrine cause

Naushira Pandya MD, CMD, FACP

71

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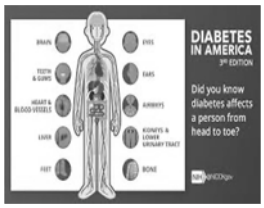
72

Diabetes Mellitus

Older adults with diabetes may exhibit one or more of the following symtoms:

- Abdominal pain
- Diarrhea
- Nausea
- Flatulence
- Vomiting
- Constipation or obstipation
- Recurrent hypoglycemia



73

Diabetes and Gastroparesis

- Gastric and intestinal motility disorders are late complications of diabetes.
- May have dysrhythmias, antral hypomotility, gastroparesis, constipation, diarrhea, fecal incontinence, and weight loss in severe cases
- Nausea is the most common; bloating, postprandial satiety, sensation of fullness, acute hypo- and hyperglycemia, and colonization with *H. pylori* are also seen.
- Gastroparesis is similar in type 1 and type 2 DM ;develops in 5–12% due to autonomic neuropathy leading to gastric hypotonia, larger postprandial antral volume, and delayed emptying (over 170 minutes), without mechanical obstruction.
- Reduces carbohydrate absorption through the release of the gut peptides such as the incretin hormones glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide
- Metformin and GLP1-RA also cause similar symptoms

Bharucha, Adil E., Yogish C. Kudva, and David O. Prichard. "Diabetic gastroparesis." *Endocrine reviews* 40.5 (2019): 1318-1352.

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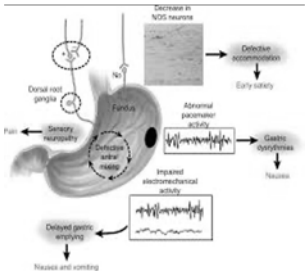


Mechanisms of Diabetic Gastroparesis

75

Diabetic diarrhea; causes of chronic diarrhea

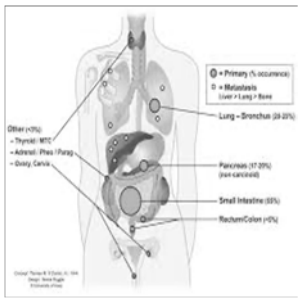
- Disordered motility of the small bowel and colon (vagal nerve dysfunction, sympathetic nerve damage, acute changes in glucose concentrations)
- Increased intestinal secretion (autonomic neuropathy of the ENS affecting mucosal water transport and ion fluxes)
- Small intestinal bacterial overgrowth (altered small bowel motility, maldigestion or malabsorption due to enterocyte damage)
- Fecal incontinence (voluminous stool, anorectal dysfunction)
- Medications (metformin, artificial sweeteners, e.g., sorbitol)
- Others (exocrine pancreatic insufficiency and celiac sprue)

76

Neuroendocrine Neoplasms (NENs) of the Gastrointestinal Tract

- Tumors originating from the tubular gastrointestinal tract and the pancreas are relatively rare with an annual incidence in the USA of 35 per 100,000 population
- The rectum and small intestine are currently the most common primary sites
- Well-differentiated neuroendocrine tumors (NETs) include carcinoid, islet cell, and pancreatic (neuro)endocrine tumors and generally have a better prognosis
- Poorly differentiated neuroendocrine carcinomas (NECs) include small-cell carcinoma and large-cell neuroendocrine carcinoma have a rapid clinical course.

77



Anatomical Distribution of Neuroendocrine Tumors

78

When to Suspect a Gastroenteropancreatic Neuroendocrine Neoplasm?

- Unexplained diarrhea
- Confirmed hypoglycemia reversed by glucose intake in the absence of pharmacological treatment for diabetes
- Recurrent peptic ulceration
- Unexplained hypokalemia
- Necrolytic migratory erythema
- Steatorrhea
- Cholelithiasis
- Unexplained flushing
- Unexplained anemia
- Weight loss

79

GI SX	Hypoth	Hyperth	HPTH	Adr Insuf	Cushing	Diabetes	NENs
Abd pain	X		X	X	X	X	X
Anorexia	X	X	X	X		X	
Nausea		X	X	X		X	
Constip	X		X			X	
Diarrhea	X	X		X		X	X
Dyspep			X			X	X
Fecal Inc		X				X	
Gastropa						X	
Int motil	X	X				X	X
Malabs	X	X	X			X	X
Peptic u			X		X		X
Vomiting		X		X		X	

80

Take Home Messages

- Older adults often present with vague and/or atypical signs and symptoms of endocrine disorders, such as weakness, depression, falls, impaired cognition, or functional decline.
- Within the GI tract, manifestations of endocrine disease may include anorexia, dysphagia, nausea and vomiting, changes in hepatobiliary function, constipation, diarrhea, and weight loss
- Changes may be misinterpreted as age-related physiologic changes, primary gastrointestinal disorders, geriatric syndromes, or as sequelae of underlying morbidities (e.g., heart failure, CAD).
- The clinician needs to maintain a high index of suspicion for an endocrine diagnosis in patients with GI symptoms that persist without reasonable explanation.

81

81

Take Home Messages

- In patients with a known endocrine disorder, it is important to exclude other causes of GI symptoms (i.e., minimize diagnostic overshadow).
- Carefully review medications used for endocrine disorders for appropriateness of dosing and potential GI adverse effects.
- Due to fragmentation of care provided by multiple specialists, a brief comprehensive geriatric assessment of the older adult is advised to evaluate all potential contributing causes (to reduce cognitive and anchoring bias).
- Management should be appropriate for the patient's goals of care and to improve quality of life.

82

82

DISCUSSION

83

83