

RUTGERS

THE STATE UNIVERSITY
OF NEW JERSEY



Annual Internal Medicine Review

ENDOCRINOLOGY

PART 2

Sara Lubitz, MD

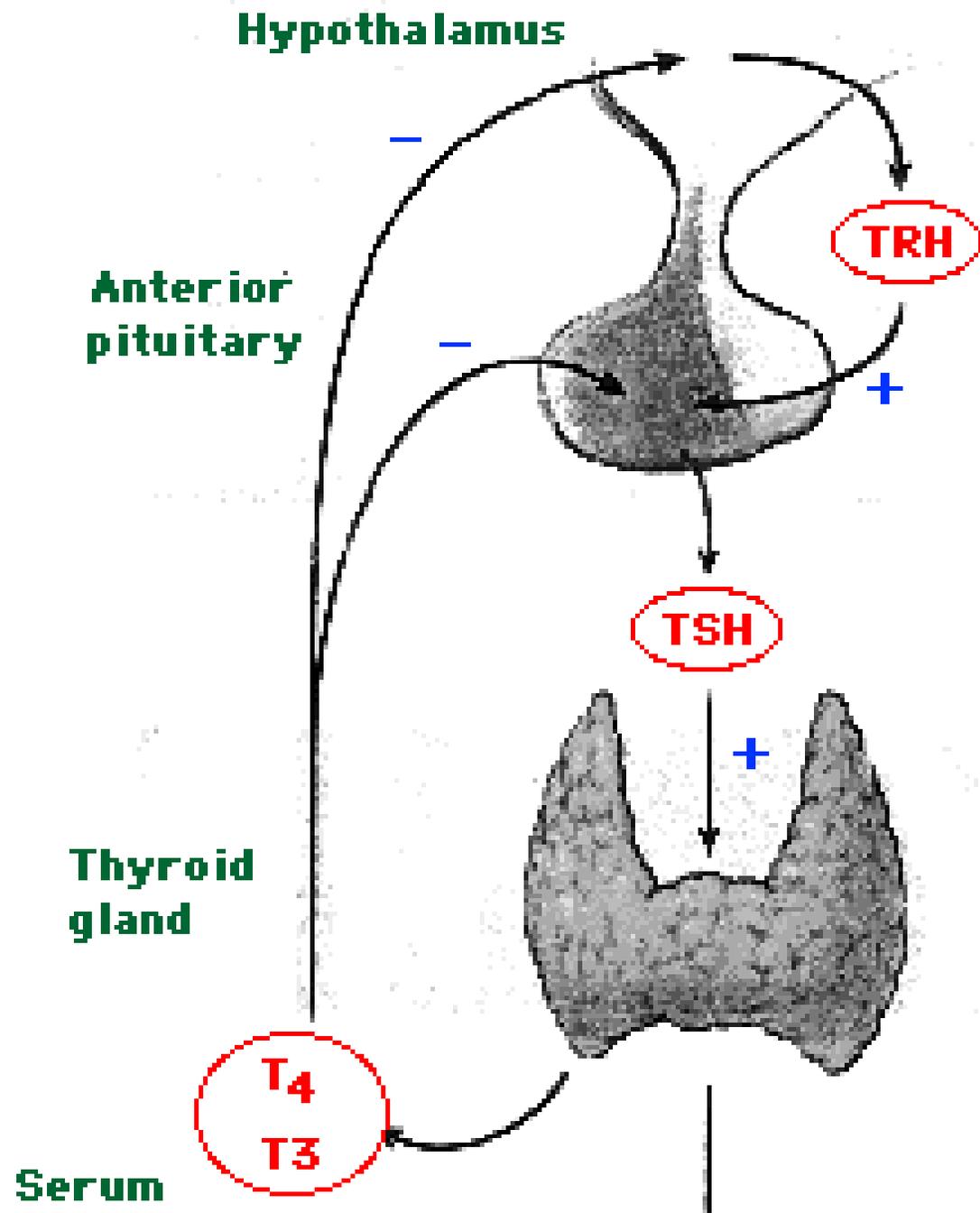
Associate Professor of Medicine

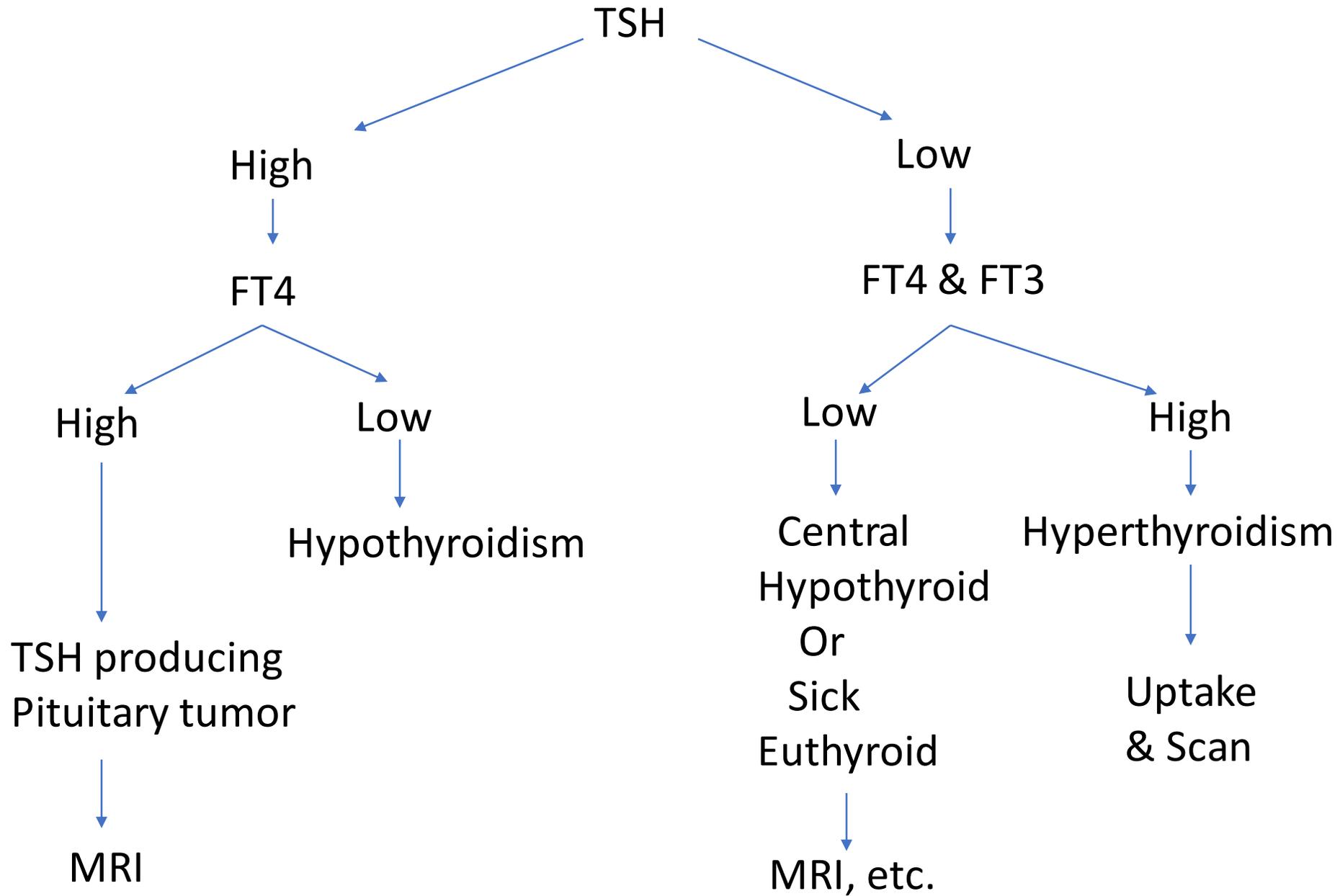
Medical Director of the Pituitary Center

Program Director, Endocrinology Fellowship

Rutgers Robert Wood Johnson Medical School

lubitzsa@rutgers.edu





Hypothyroidism: Blood Tests

BEST SCREENING TEST FOR DISEASE: TSH

TO CONFIRM HYPOTHYROIDISM: TSH & FT4

***IF PITUITARY HYPOTHYROIDISM TSH MAY BE HIGH,
LOW OR NORMAL - FOLLOW T3 AND T4 LEVELS***

Hypothyroidism: Other Lab Abnormalities

- Decreased sodium
- Retention of CO₂
- Macrocytosis
- Transaminitis
- Hyperlipidemia
- Elevated prolactin

Hypothyroidism

- Differential Diagnosis

- Iodine Deficiency – most common cause world wide
- Hashimoto's – most common cause in US
- Thyroiditis (hypothyroid phase)
- Post-Surgery or Post-Radiation
- Drug Induced
 - Lithium
 - Amiodarone
 - Interferon
 - Sunitinib
 - Immune checkpoint inhibitors
- Iodine induced
- Synthetic defects
- Pituitary hypothyroidism (secondary)

Hashimoto's Disease

- Most common cause of hypothyroidism in North America
- Autoimmune (Chronic) lymphocytic thyroiditis
- Antithyroid antibodies:
 - Thyroperoxidase (TPO) Antibody (previously microsomal antibody)
 - Thyroglobulin (Tg) Antibody
- Females > Males
- Runs in families with other autoimmune disease

Question 1

- A 75-year-old woman is admitted to the medical intensive care unit with progressive obtundation. Physical examination reveals a nonarousable elderly woman, with core temperature of 95 °F, blood pressure of 104/84 mm Hg, and pulse rate of 48/min. The patient weighs 82 kg and has a 4-cm transverse scar above the suprasternal notch, cold doughy skin, and delayed deep tendon reflex relaxation phase.
- The patient's medical records state that she is taking both digoxin and levothyroxine, but she has not been seen in more than a year.
- Serum sodium is 127 meq/L; total cholesterol is 318 mg/dL. Digoxin is undetectable. Serum TSH is pending. Urinalysis shows too many leukocytes to count and gram-negative rods. Urine and blood cultures are pending.

Question 1

Which of the following would be appropriate therapy at this time?

- A. Levothyroxine, corticosteroids, empiric antibiotics
- B. Levothyroxine alone
- C. Levothyroxine and liothyronine
- D. No therapy until TSH level is known

Myxedema Coma

- Definition: loss of brain function as a result of severe, longstanding low level of thyroid hormones. Myxedema coma is considered life-threatening
- Most common in elderly patients during winter months
- Symptoms: Hypothermia, Mental Depression, Edema, Bradycardia, Pleural or Cardiac Effusions
- Treatment: IV levothyroxine + Steroids (if adrenal insufficiency is a possibility)

Question 2

- A 67-year-old woman requests treatment for “thyroid”. She has fatigue and difficulty losing weight and read that this can be due to low thyroid. Her medical history is positive for depression which is well controlled. Her mother had hypothyroidism and her father had a MI at age 55. Her only medication is fluoxetine.
- On physical examination, the blood pressure is 142/88 mm Hg, pulse rate 64/min, and BMI 28.1. Her thyroid gland is not enlarged. Her skin is dry. Her reflexes are normal.
- Laboratory Studies:
 - CBC and BMP normal
 - Cholesterol 235 mg/dL Triglycerides 118 mg/dL
 - HDL 35 mg/dL LDL 166 mg/dL
 - TSH 7.2 μ U/mL
 - TSH (repeat 6 weeks later) 7.8 μ U/mL
 - Free T4 (at time of 2nd TSH) 1.0 ng/dL

Question 2

Which of the following is expected to improve by starting thyroid hormone replacement therapy (levothyroxine) in this patient?

- A. Weight
- B. Blood Pressure
- C. HDL cholesterol
- D. Fatigue
- E. TSH level

Subclinical Hypothyroidism

- TSH elevated and Free T4 in normal range
- Rate of progression to overt hypothyroidism 5-20% per year if TPO antibody positive
- Consider treatment only if
 - TSH > 10 (normal range .5-4.5 mIU/L)
 - Goiter
 - Very symptomatic
 - Planning pregnancy (TSH <2.5)

Question 3

- A 28-year-old student, previously in good health, notes pain and tenderness in his neck for the past two weeks. During this time he noted fatigue, poor appetite, and felt feverish.
- His pulse is 92 beats/min; BP 130/56 mm Hg; temperature 100°F; weight 77 kg; height 5'11. He is very fidgety. He has a stare and lid lag but no proptosis. His thyroid is enlarged with firm consistency-the left lobe is tender. Cardiac examination shows a forceful PMI with normal heart sounds and no murmur. Deep tendon reflexes are very brisk. The rest of the examination was unremarkable.
- Laboratory tests revealed:
 - Serum T4 = 21.1 µg/dL (normal = 5 to 12 µg/dL)
 - Serum T3 = 302 ng/dL (normal = 80 to 175 ng/dL)
 - Serum TSH <0.05 µIU/mL (normal = 0.4 to 4.5 µIU/mL)
 - CBC and routine blood chemistries - normal

Question 3

What is the most likely diagnosis?

- A. Subacute (de Quervain's) Thyroiditis
- B. Grave's Disease
- C. Toxic multinodular goiter
- D. Factitious Hyperthyroidism

Question 4

To confirm your diagnostic impression, which is the best next test to obtain?

- A. Thyroglobulin
- B. Anti-thyroid antibodies
- C. Thyroid radioiodine uptake and scan
- D. Thyroid ultrasound exam

Hyperthyroidism: blood tests

BEST SCREENING TEST FOR DISEASE: TSH

TO CONFIRM HYPERTHYROIDISM: TSH, FT4, T3

Hyperthyroidism: Differential Diagnosis

- Graves' Disease
- Thyroiditis
- Autonomous Toxic Nodule
- Toxic Multinodular Goiter
- Iodine Induced
- TSH producing pituitary tumor
- Ingestion of thyroid hormone
- Struma Ovarii

Graves' Disease

- Classic Exam: Goiter, Proptosis, Pre-tibial Myxedema
- Graves ophthalmopathy may occur before, at the same time as, or after the symptoms of Graves Disease
 - Treated with steroids or surgery
 - Radioactive iodine treatment of hyperthyroidism may make eye disease worse (especially smokers)



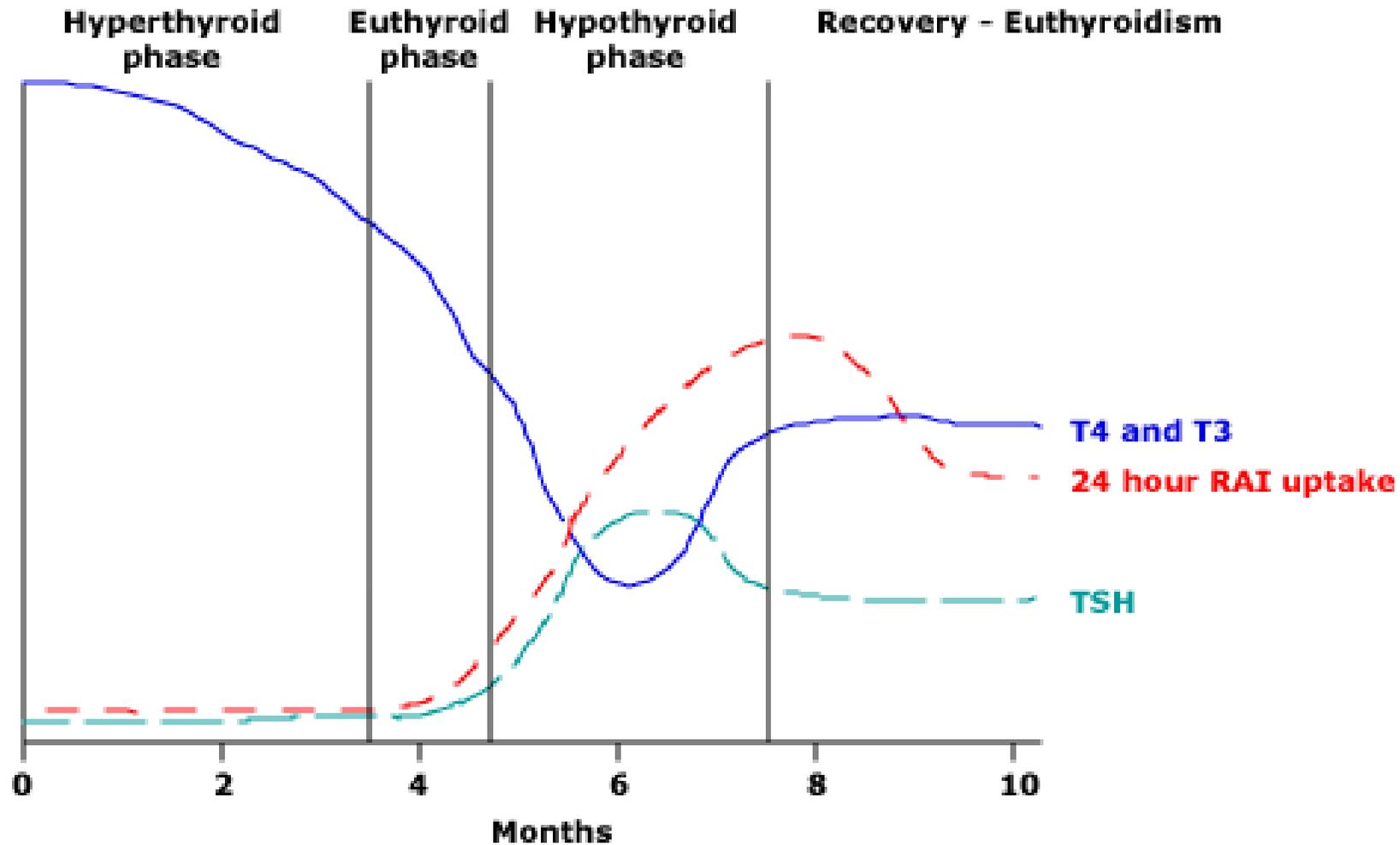
Thyroiditis

Definition: Inflammation of the thyroid with transient hyperthyroidism due to release of pre-formed hormone from the colloid space. This initial presentation is followed by a hypothyroid phase and then usually a recovery of thyroid function

Causes:

- Post-partum
- Silent
- DeQuervain's (subacute)
- Acute (bacterial infection)
- Drugs: Amiodarone, Sunitinib, Interferon-alpha, PD1 inhibitors
- Radiation

Characteristic Time Course of Thyroiditis



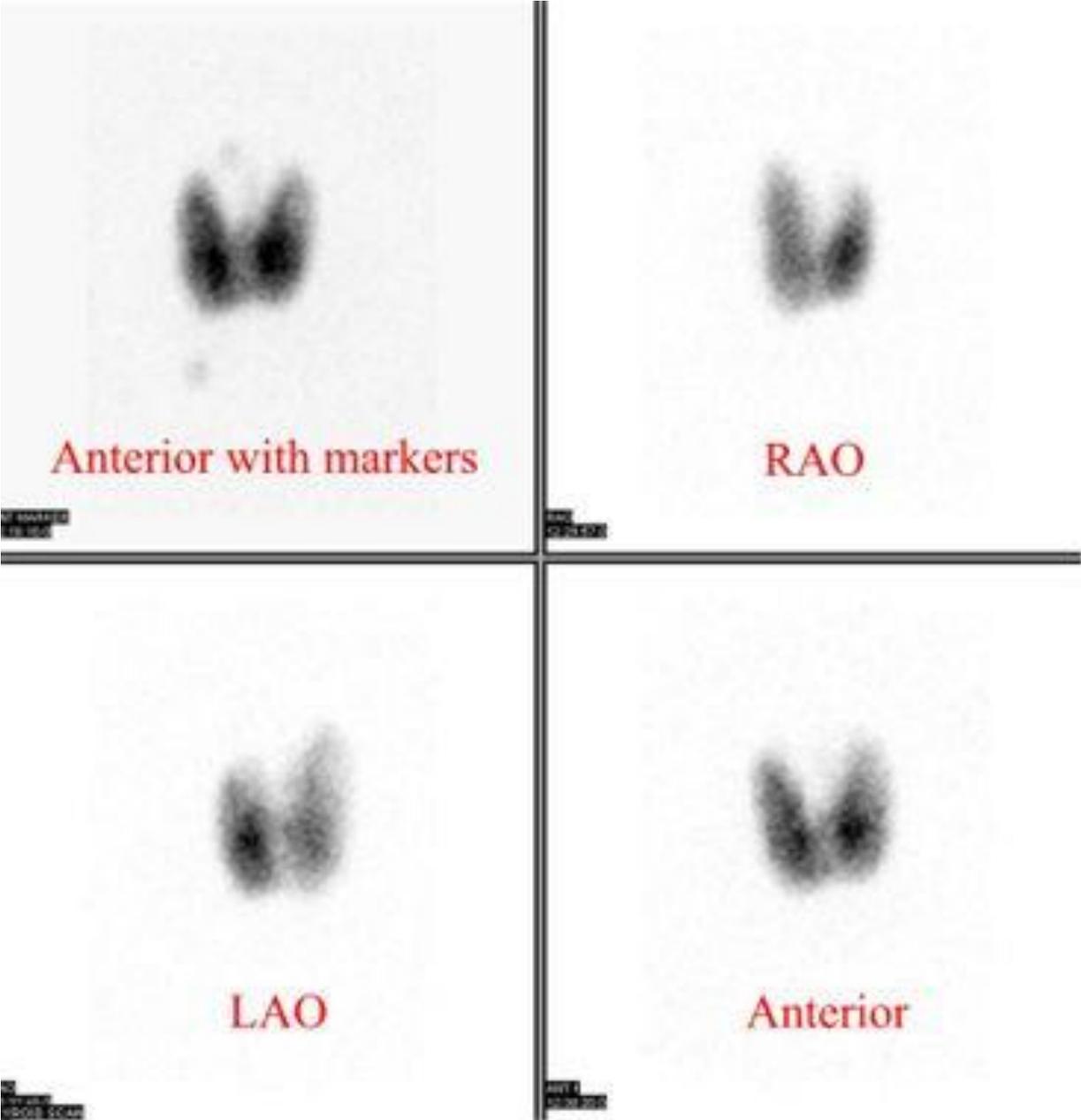
Subacute (de Quervain's) Thyroiditis

- Preceding viral infection (URI, influenza)
- Infiltration of the gland with granulomas
- Painful goiter
- Elevated ESR
- Fever
- Hyperthyroid phase → Hypothyroid phase
- Treat with beta-blockers, ASA, NSAIDS +/- steroids

Hyperthyroidism Diagnosis

- Next step after history and exam if NOT pregnant or breastfeeding is Radioactive Iodine Uptake and Scan
 - Thyrotoxicosis with High Uptake:
 - Graves
 - Multinodular Goiter
 - Autonomous Nodule
 - Thyrotoxicosis with Low Uptake (almost zero%):
 - Thyroiditis
 - Exogenous thyroid hormone ingestion

Uptake 65% and Scan Consistent with Graves Disease



Uptake (55%) and Scan Consistent with Multinodular Goiter



Question 5

A 23-year-old woman is diagnosed with Graves' disease. She is 6 months post-partum and is breastfeeding her infant and wishes to continue. There is no proptosis. Thyroid gland is 1.5 times the normal size. The remainder of the examination is normal.

- Laboratory tests revealed:
 - Serum TSH <0.05 $\mu\text{IU/mL}$ (normal = 0.4 to 4.5 $\mu\text{IU/mL}$)
 - Serum FT4 = 2.3 $\mu\text{g/dL}$ (normal = 0.8 to 1.7 $\mu\text{g/dL}$)
 - CBC and routine blood chemistries - normal

Question 5

Which of the following is the most appropriate treatment ?

- A. Atenolol
- B. Prednisone
- C. Methimazole
- D. Radioactive iodine
- E. Thyroidectomy

Thyrotoxicosis: Treatment

- Beta-blockers (hyperadrenergic symptoms)
- Hyperthyroidism:
 - Anti-thyroid Drugs
 - Propylthiouracil (PTU)
 - Methimazole
 - Radioiodine Ablation
 - Surgical Thyroidectomy
- Thyroiditis:
 - ASA, NSAIDS, +/- corticosteroids
- Iodine (high doses → Wolff Chaikoff effect)

Antithyroid Drugs

- PTU (propylthiouricil)
 - Blocks thyroperoxidase enzyme (can't make thyroxine)
 - Inhibits 5'deiodinase activity (can't convert T4 to T3)
 - Side Effects: Agranulocytosis, Rash, Hepatotoxicity
 - Drug of choice during first trimester pregnancy
 - Used during thyroid storm (decreases T4 to T3 conversion)
- Methimazole
 - Blocks thyroperoxidase enzyme (can't make thyroxine)
 - Side Effects: Agranulocytosis, Rash
 - First Line Drug of Choice (new since 2009)
 - Aplasia Cutis if used 1st trimester

Subclinical Hyperthyroidism

- TSH low with Ft4 normal and T3 normal
- Treatment
 - Antithyroid drug trial
 - Radioactive Iodine
 - Surgery
- Only treat if
 - TSH undetectable (<0.01) (normal 0.5-5mIU/L)
 - Elderly patient at risk for atrial fibrillation
 - Elderly patient at risk for osteoporosis

Thyroid Storm

- Hyperthyroid Crisis: Medical Emergency
- Mortality 20%
- Symptoms:
 - Fever, Tachycardia, Heart Failure, Nausea, Vomiting, Diarrhea, Mental Status Changes
- Treatment:
 - IV Fluids
 - Beta-Blockers
 - High dose PTU or Methimazole
 - Steroids
 - Iodine Drops (SSKI, Lugol's Solution)
 - Thyroidectomy

Question 6

A 60-year-old man is evaluated for palpitations, heat intolerance, and a 2.4-kg weight loss over 1 month. The patient has a history of dilated cardiomyopathy and congestive heart failure, and his medications include warfarin, digoxin, lisinopril, and carvedilol. On physical examination, the pulse is 82/min and regular, the thyroid gland is twice normal size, and he has a moderate resting tremor.

Laboratory testing shows free T4 3.1 ng/dL (normal 0.9-2.3) and TSH <0.01 μ U/mL (normal 0.5-4.5)

Question 6

Which of the following changes in his therapeutic regimen should be made while he remains thyrotoxic?

- A. Decrease both warfarin and digoxin doses
- B. Increase both warfarin and digoxin doses
- C. Increase warfarin dose, decrease digoxin dose
- D. Decrease warfarin dose, increase digoxin dose
- E. No change in warfarin or digoxin dose

Hyperthyroidism and Drug Metabolism

- Hyperthyroidism INCREASES the metabolism of most drugs so you would need a HIGHER dose or more frequent dosing Ex. Anti-seizure medication

EXCEPT

- Hyperthyroidism increases metabolism of clotting factors so you need a LOWER dose of warfarin to get to goal INR

Question 7

A 64-year old woman has been in the ICU for the past 2 weeks. She is currently being treated for a ventilator associated pneumonia and develops rapid atrial fibrillation. As part the work-up for A-fib thyroid function tests are drawn. Her blood tests show TSH 0.3 μ U/mL (nl 0.5-4.5) free T4 0.7 ng/dL (nl 0.9-2.3) and T3 63 ng/dL (nl 80-200)

Question 7

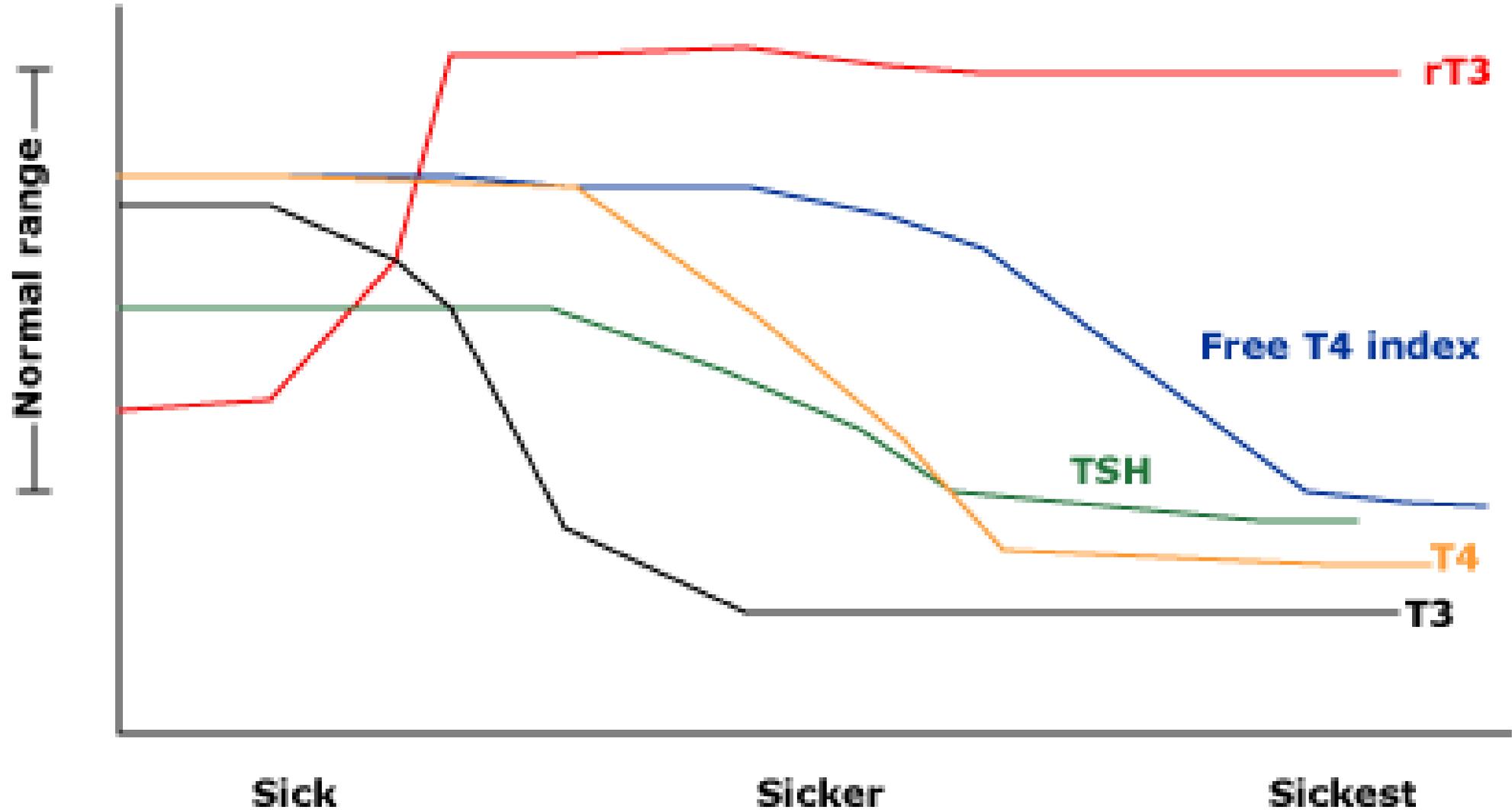
This patient most likely has:

- A. Subclinical Hypothyroidism
- B. Euthyroid sick syndrome
- C. Graves' disease
- D. Hashimoto's thyroiditis
- E. Subacute thyroiditis

Sick Euthyroid: AKA Euthyroid Sick Syndrome

Syndrome of abnormal findings on thyroid function tests that occur in the setting of a “nonthyroidal illness” without preexisting hypothalamic-pituitary and thyroid gland dysfunction. After recovery from the illness, these thyroid function test result abnormalities should be completely reversible

Sick Euthyroid Syndrome



Goiter

- Symmetric
- Uni-nodular
- Multinodular
- Causes:
 - Hyperthyroidism
 - Hypothyroidism
 - Familial



Pemberton Sign



From Wallace, C. et. al. *Ann Intern Med* 1996;125:568-569

Question 8

A 33-year-old man is evaluated for a mass in the right side of his neck that he noticed while shaving. He has had no neck pain, hoarseness, or dysphagia. He has no family history of thyroid disease. On physical examination, he has a large right thyroid nodule that is moderately mobile and nontender. There are no palpable cervical lymph nodes. You send him for a thyroid ultrasound which shows a 2.5 cm hypoechoic nodule in the right mid pole with internal vascularity and no calcifications.

Question 8

Which is the best next test to do in the evaluation of his thyroid nodule?

- A. Fine Needle Aspiration of the Nodule
- B. Serum Thyroid Stimulating Hormone
- C. CT Scan of the Neck with Contrast
- D. Anti-thyroglobulin Antibody
- E. Right hemithyroidectomy

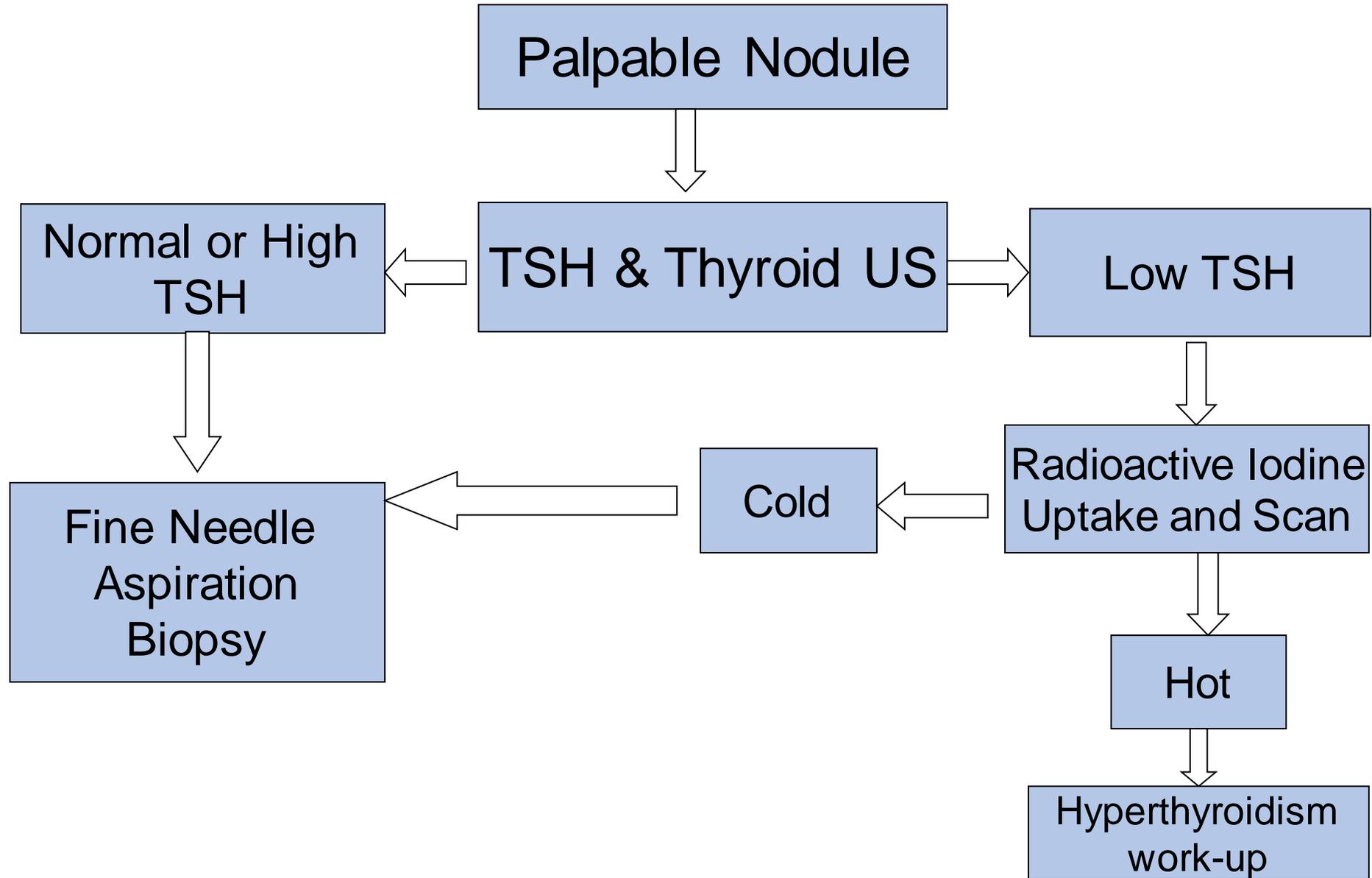
Thyroid nodules

- Thyroid nodules are common
 - 10% lifetime probability of developing a palpable nodule
 - U/S: 20% of women have nodules
 - U/S: 50% of women > 50 y.o. have nodules
- Most thyroid nodules are benign
 - Only 5 - 10 % are cancer
 - 92 % Differentiated thyroid cancer
 - Papillary Thyroid Cancer
 - Follicular Thyroid Cancer

Thyroid nodules

- Complications
 - Compressive symptoms
 - Autonomous Function/Hyperthyroidism
 - Cancer
- Diagnosis
 - TSH
 - Thyroid Ultrasound

Thyroid nodules



Question 9

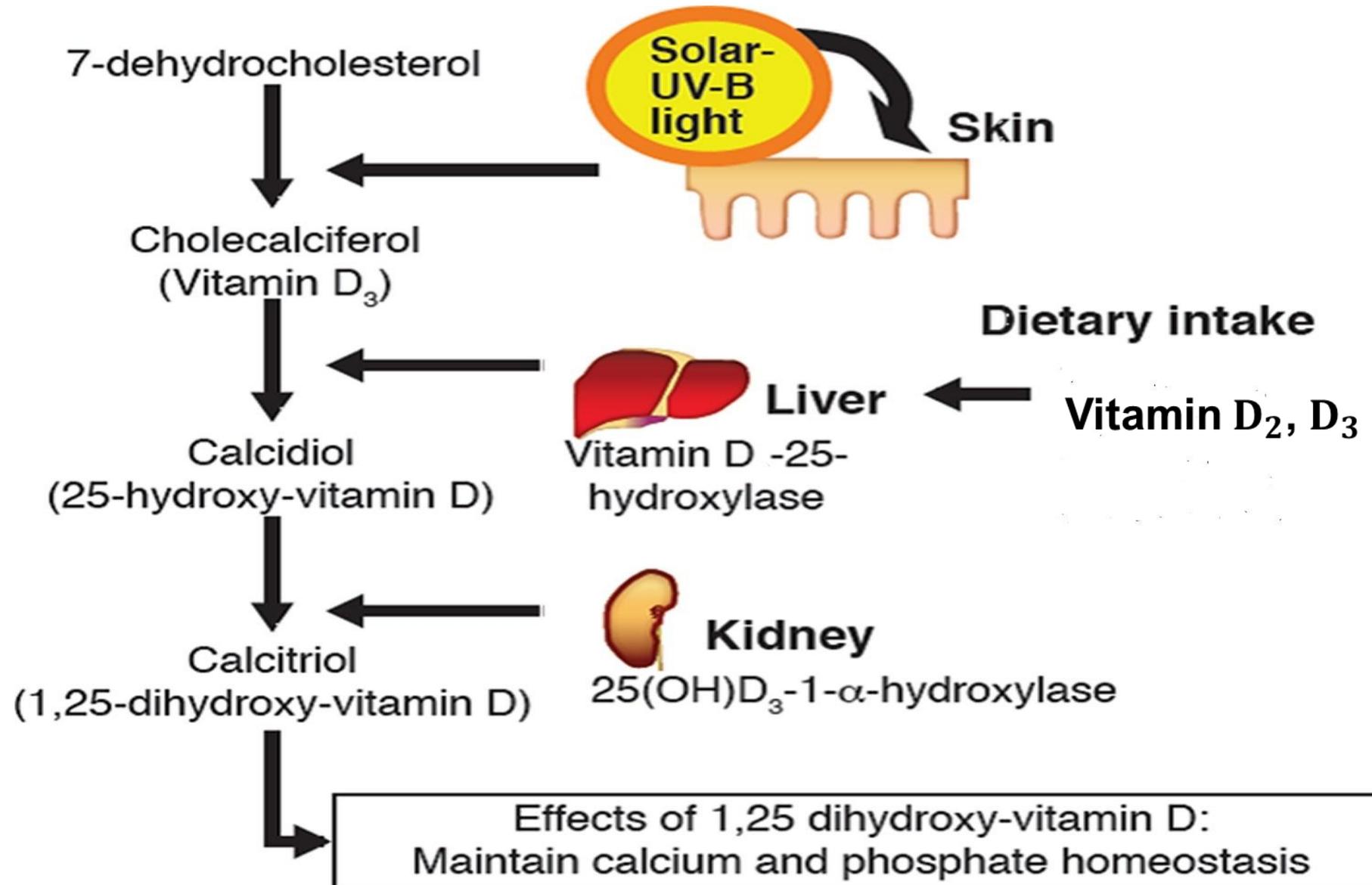
A 32-year old female presents with muscle aches and lethargy. On further history she reports that she wears SPF 55 sunblock at all times due to a family history of melanoma. She is lactose intolerant and avoids dairy products. You are suspecting Vitamin D deficiency.

Question 9

What would the best test be to establish the diagnosis?

- A. Calcitonin level
- B. Serum calcium level
- C. 1, 25-dihydroxycholecalciferol level
- D. 25-hydroxycholecalciferol level

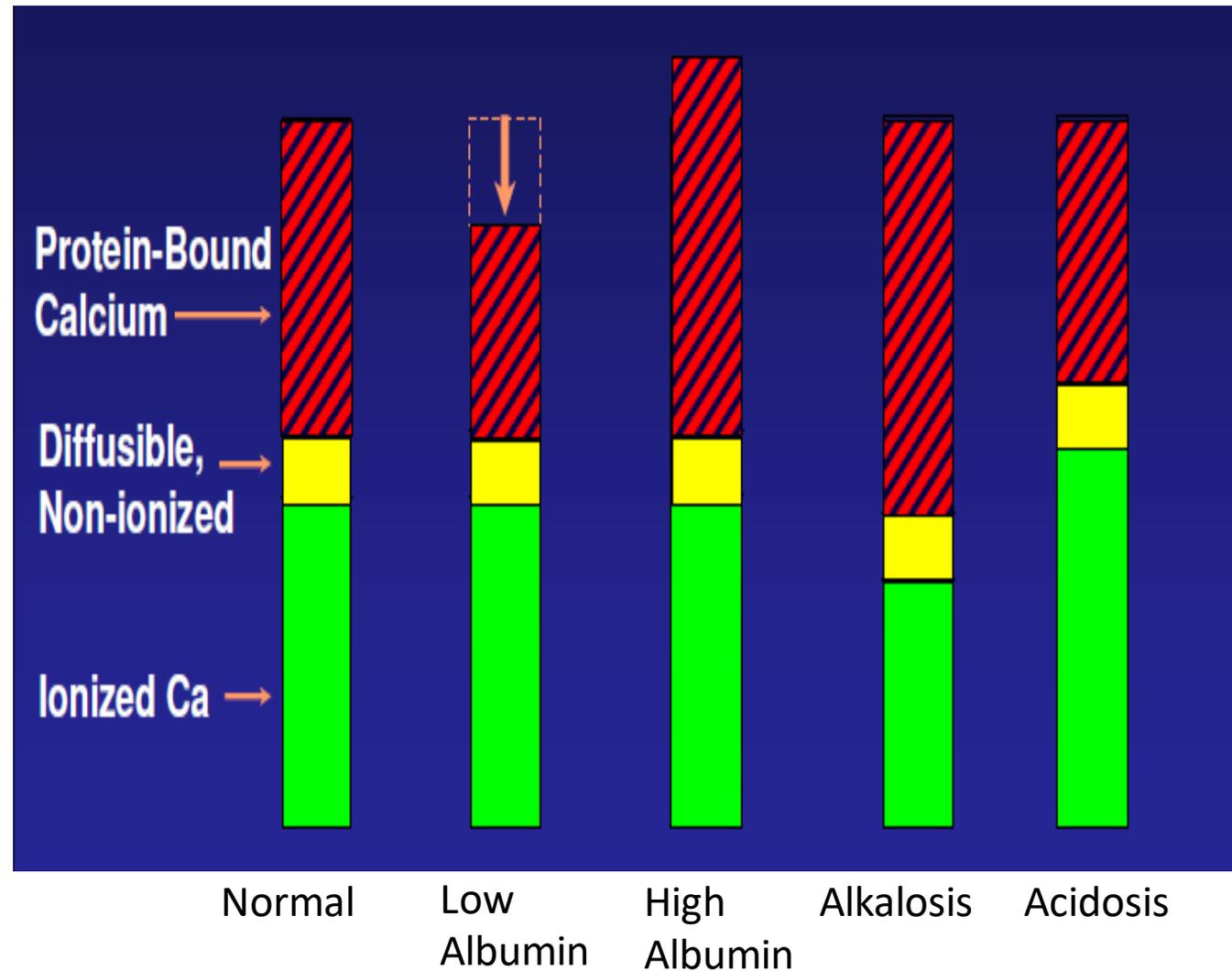
Vitamin D Production & Metabolism



Calcium Metabolism

- Parathyroid Hormone
 - Promotes resorption of calcium from bone
 - Increases calcium resorption in kidneys
 - Activates 1 alpha hydroxylase in kidneys
- Calcitriol ($1\alpha,25$ – dihydroxy vitamin D3)
 - Increases calcium absorption in intestines
- Calcitonin
 - Produced by the parafollicular or C cells of the thyroid interstitium
 - Promotes a decrease in circulating calcium

Albumin and pH Influence on Serum Calcium Concentration



Question 10

- A 22-year-old woman is evaluated for perioral and fingertip paresthesias, lightheadedness and hand cramping. She reports a history of anxiety. Two days ago she underwent a thyroidectomy for papillary thyroid cancer.
- Laboratory studies: albumin 4.5 g/dL (3.4-5), calcium 6.9 mg/dL (8.6-10.3), phosphorous 3.9 mg/dL (3.4-4.5)

Question 10

Which of the following is the most appropriate next step in the management of this patient?

- A. Intravenous calcitriol
- B. Intravenous bisphosphonate
- C. Intravenous calcium gluconate
- D. Oral ergocalciferol 50,000 IU daily
- E. Oral calcium carbonate 1200mg Q6

Hypocalcemia

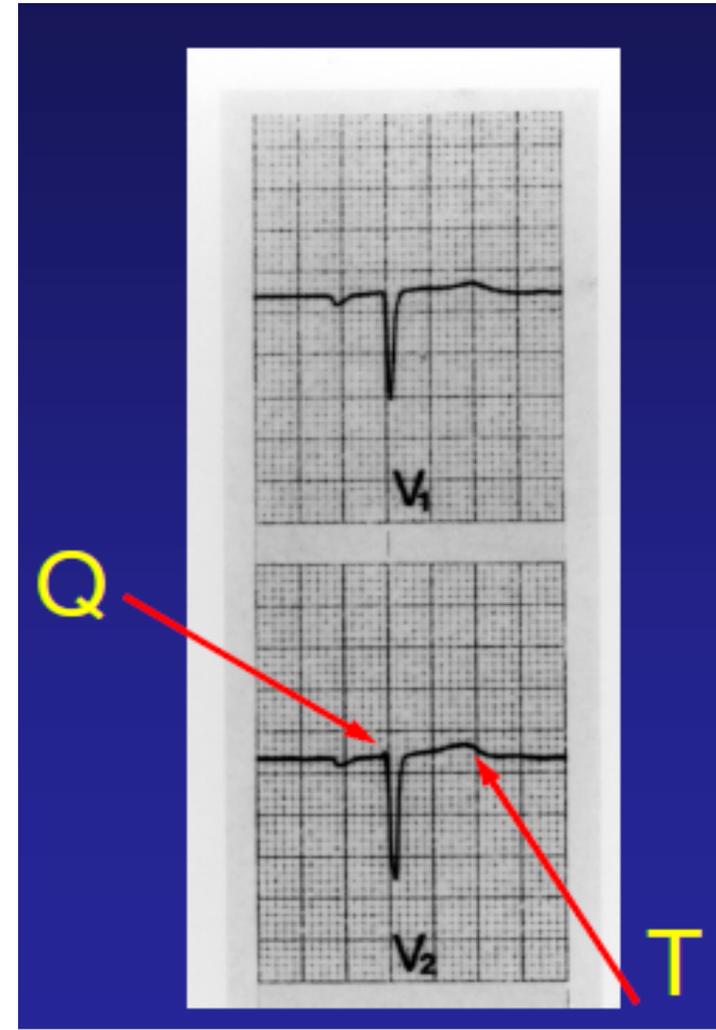
- Deficient Vitamin D supply or activation
 - Malabsorption
 - Renal Failure
 - Liver Failure
 - Hypoparathyroidism
- Renal Failure
- Chelating agents: **Citrate in multiple transfusions**
- Deficient synthesis or secretion of PTH
- Deficient PTH action (PTH resistance)
 - Pseudohypoparathyroidism

Hypocalcemia: Signs and Symptoms

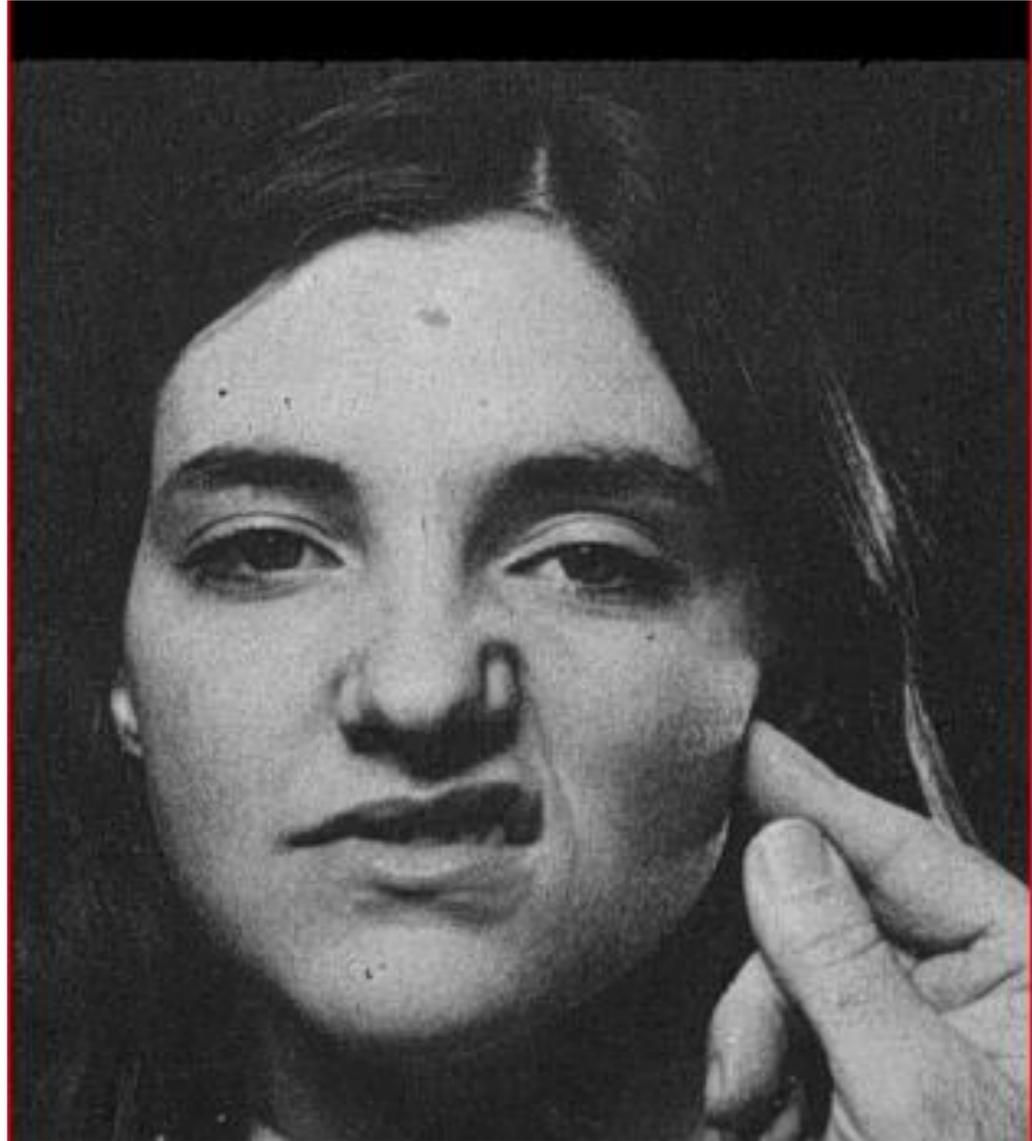
- Neuromuscular Irritability
 - Paresthesias: circumoral, fingers, and toes
 - Carpal-pedal spasm: Trousseau sign
 - Laryngospasm, Bronchospasm
 - Tetany
- Central Nervous System
 - Seizures
 - Increased intracranial pressure with papilledema
 - Extrapyrarnidal disturbance
- Abnormalities of teeth, nails, skin and hair

Hypocalcemia: Signs and Symptoms

- Cardiovascular
 - Prolonged QT interval
 - Heart Block
 - Congestive heart failure
- Ophthalmologic
 - Papilledema
 - Lenticular cataracts
- Dystrophic Calcification



Tetany: Chvostek Sign



Carpal Spasm: Trousseau Sign



Chronic Renal Failure

- Most Common Cause of Hypocalcemia
- Pathophysiology
 - Hyperphosphatemia
 - Reduced 1,25 (OH) Vitamin D (calcitriol)
 - Impaired sensitivity of the skeleton to PTH
- Patients can develop secondary hyperparathyroidism and parathyroid gland hyperplasia

Vitamin D Deficiency & Resistance

- Failure to mineralize bone
 - Rickets
 - Osteomalacia
 - Labs → ↓ calcium, ↓ phosphorus, ↑ serum alkaline phosphatase
- Pathophysiology
 - Vitamin D Deficiency
 - No sunlight exposure or dairy in diet
 - Intestinal malabsorption **Ex. Celiac Disease**
 - Drugs: INH, rifampin, phenobarbital, carbamazepine
 - Reduced 1,25 Hydroxylase activity
 - Resistance to 1,25(OH)D (calcitriol) action
 - Hypophosphatemic Rickets



Hypoparathyroidism

- Labs: Hypocalcemia and Hyperphosphatemia
- Causes
 - Surgical Removal or Injury (most common cause, can occur during thyroid surgery)
 - Autoimmune (autoimmune polyglandular syndrome Type1)
 - PTH resistance (pseudohypoparathyroidism)
 - Hypomagnesemia
 - DiGeorge's Syndrome
 - Mutation of the calcium-sensing receptor

Pseudohypoparathyroidism

- PTH resistance
 - High PTH
 - Low Calcium
 - High Phosphate
 - Based on classic phenotype
- Pseudopseudohypoparathyroidism
 - Classic phenotype without lab abnormalities
 - Paternal imprinting



Treatment of Hypocalcemia

- Acute symptomatic hypocalcemia → IV calcium gluconate
- Chronic hypocalcemia → Oral calcium and vitamin D
- Vitamin D deficiency → cholecalciferol (D₃) or ergocalciferol (D₂)
 - Each additional 100 IU of vitamin D₃ consumed per day will raise 25OHD levels by 1 ng/ml (2.5 nmol/l)
- Kidney disease
 - eGFR ≥ 30 mL/min/1.73 m² → vitamin D₃ or vitamin D₂
 - eGFR < 30 mL/min/1.73 m² → calcitriol (1,25-dihydroxyvitamin D)
- Liver disease → calcidiol (25-hydroxycholecalciferol)
- Hypoparathyroidism → calcitriol (1,25- dihydroxyvitamin D)

Question 11

A 48-year-old woman is evaluated for a serum calcium concentration of 11.7 mg/dL discovered on routine screening. A dual-energy x-ray absorptiometry showed T scores at the lumbar spine and left femoral neck of -0.88 and -0.05 respectively. There is no history or evidence of renal stones, bone fracture, cognitive impairment, or fatigue. The intact serum parathyroid hormone level is 115 pg/mL (nl 11-54). The serum creatinine is 0.9 mg/dL. The urine calcium/creatinine clearance ratio is greater than 0.01, and the 24-hour urine calcium excretion is 250 mg (nl 100-300).

Question 11

Which of the following is the most appropriate next step in the management of this patient?

- A. Observation
- B. Intravenous bisphosphonate
- C. Mammography
- D. Parathyroidectomy
- E. Low-calcium diet

Hypercalcemia

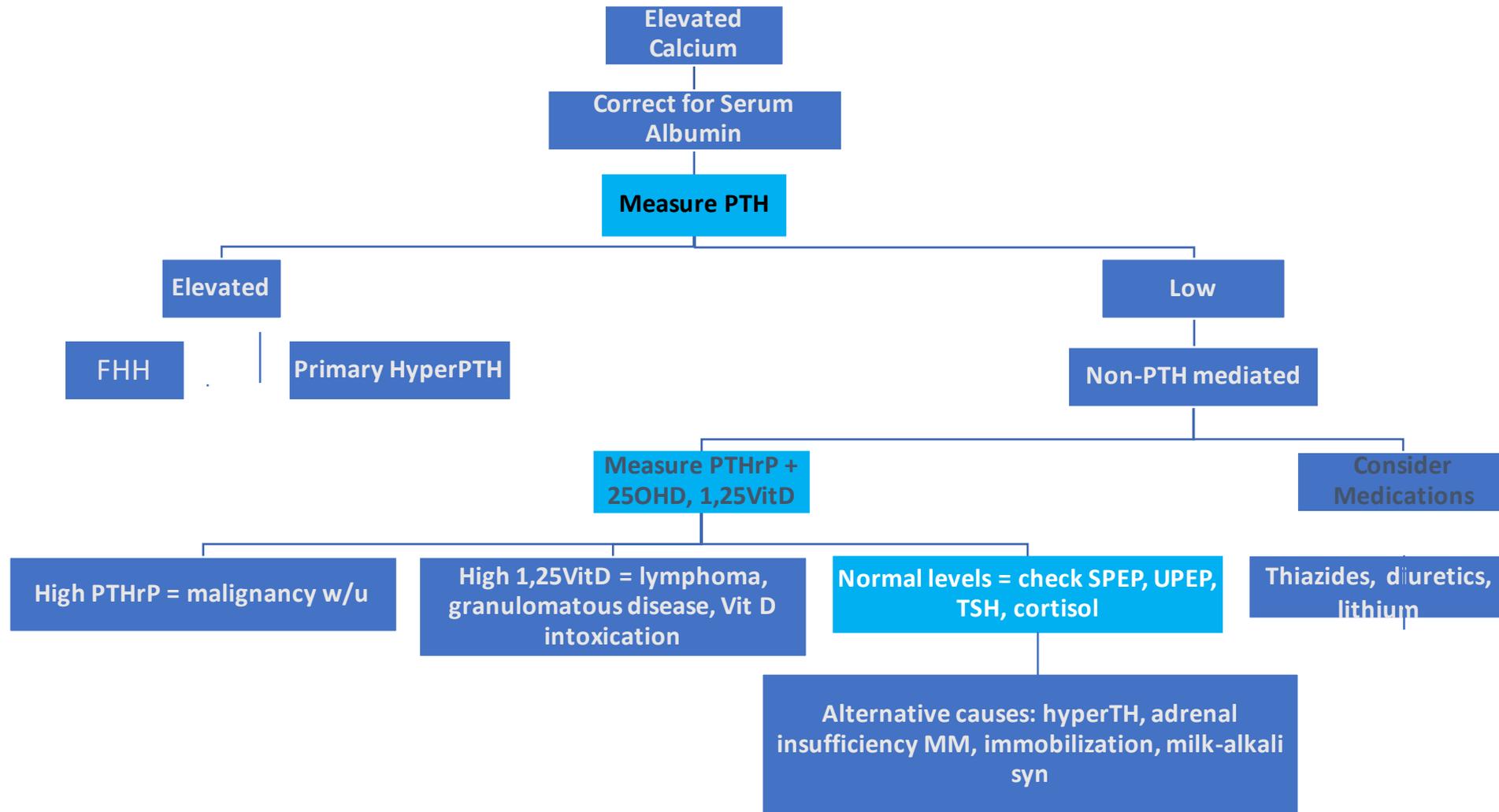
- Causes:
 - Primary Hyperparathyroidism
 - Malignant Disease
 - Sarcoidosis, tuberculosis or other granulomas
 - Hyperthyroidism
 - Milk-Alkali Syndrome
 - Familial Hypocalciuric Hypercalcemia
 - Adrenal Insufficiency
 - Drugs:
 - Vitamin D intoxication
 - Vitamin A intoxication
 - Thiazide diuretics
 - Lithium

Hypercalcemia Signs & Symptoms

- CNS
 - Lethargy
 - Confusion and inability to concentrate
 - Coma
- Gastrointestinal
 - Nausea/Vomiting
 - Constipation
 - Pancreatitis
- Renal
 - Polyuria, Polydipsia
 - Stones
- Cardiovascular
 - Short QT interval
- Skeletal
 - Arthralgia and Bone pain
 - Bone cysts

**Stones, bones,
groans, psychiatric
overtones**

Hypercalcemia Diagnosis



Familial Hyperparathyroidism Syndromes

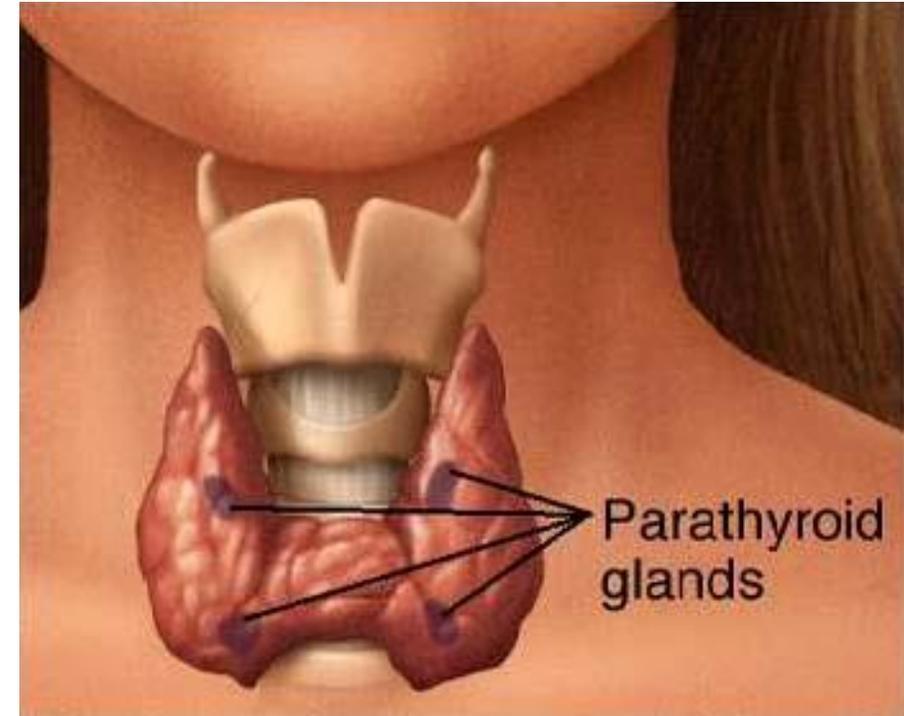
	FHH	MEN 1	MEN2a
Tissues affected	Parathyroid Kidney	Parathyroid Pituitary Pancreas	MTC Pheo Parathyroid
Presentation	↑ calcium	↑ calcium	MTC
Gene defect	<i>CaSR</i>	<i>MEN1</i> gene 11q13 * <i>CDKN1B</i> <i>P27^{kip}</i>	<i>Ret</i>

Familial Hypocalciuric Hypercalcemia

- Present from Birth
- Autosomal Dominant Inheritance
- FHx of “failed” parathyroidectomy
- Most common: Inactivating mutation of the calcium-sensing-receptor
- Enhanced reabsorption of calcium in the renal proximal tubule even in the absence of PTH
- Inappropriate PTH secretion despite hypercalcemia
- Diagnosis: urinary calcium creatinine clearance ratio of <0.01
- Benign natural history

Hyperparathyroidism

- **Primary**
 - Solitary Adenoma (85%)
 - Multiglandular hyperplasia (10-15%)
 - Carcinoma (<1%)
- **Secondary**
 - Vitamin D Deficiency
 - Renal Disease
 - Chronic Hyperphosphatemia
 - Chronic Hypocalcemia
- **Tertiary**
 - Long standing secondary HPT leading to autonomous function



Primary Hyperparathyroidism

- Indications for Surgery:
 - Symptoms (kidney stones, pain etc.)
 - Age <50
 - Serum Calcium > 1mg/dL above the upper limit of normal
 - Bone mineral density at the lumbar spine, hip, or distal radius T score < -2.5
 - Creatinine Clearance < 60ml/min
 - 24 hr urine calcium >400mg/day
 - Presence of nephrolithiasis by x-ray, US or CT

Primary Hyperparathyroidism

- Medical Management:
 - Monitor calcium yearly
 - Monitor BMD at 3 sites every 1-2 years
 - eGFR and serum creatinine yearly

 - Maintain Hydration
 - Bisphosphonates, Estrogens, and SERMs can improve BMD
 - Calcimimetic Agents (Cinacalcet)

Question 12

- A 68-year-old man with a history of metastatic lung cancer has a 3-week history of worsening fatigue, anorexia, thirst, polydipsia, and polyuria. In the ER BP is 90/60 mm Hg, HR is 114/min.
- On initial labs Serum calcium is 13.5 mg/dL (8.6-10.3), serum creatinine is 2.9 mg/dL (0.74-1.3), PTH is undetectable (8-24).
- He is treated urgently with IV hydration

Question 12

Which of the following is the best long-term therapy for the hypercalcemia?

- A. Cinacalcet
- B. Intravenous bisphosphonate
- C. Prednisone
- D. Parathyroidectomy
- E. Low-calcium diet

Hypercalcemia of Malignancy

1. Metastases with local release of cytokines (including osteoclast activating factors)
2. Tumor secretion of parathyroid hormone-related protein (PTHrP)
 - Shares the same N-terminal end as parathyroid hormone and therefore it can bind to the same receptor
 - Common in squamous cell carcinomas
3. Tumor production of 1,25-dihydroxyVitD

Treatment of Hypercalcemia

- Hydration
 - Restoration of intravascular volume reduces hypercalcemia
- Furosemide
 - Loop diuretics facilitate sodium and calcium excretion
 - Only use after intravascular volume is restored
- Bisphosphonates
 - Inhibits osteoclast bone resorption
 - IV infusion
 - Effect seen in 1 to 2 days
- Calcitonin
 - Inhibits osteoclast bone resorption
 - Works quickly but tachyphylaxis develops in a few days
- Glucocorticoids
 - High doses to treat granulomatous disease, Vitamin D intoxication, hematologic malignancies

Question 13



A 82-year-old female reports that she “keeps shrinking”. She also complains of back pain. You do a full history and exam and send her for x-rays of her spine and a DEXA scan.

Question 13

All of the following findings would meet the diagnostic criteria for Osteoporosis **EXCEPT**:

- A. DEXA scan T score -3.1
- B. Vertebral fracture on x-ray at T12
- C. DEXA scan T score -1.5
- D. History of left hip fracture 5 years ago after stumbling over a loose rug

Risk Factors for Osteoporotic Fracture

- Low Bone Mineral Density
- Advanced Age
- Previous Fracture
- History of Osteoporosis or Fracture in First Degree Relative
- Smoking
- Excessive Alcohol
- Low Weight
- Rheumatoid Arthritis

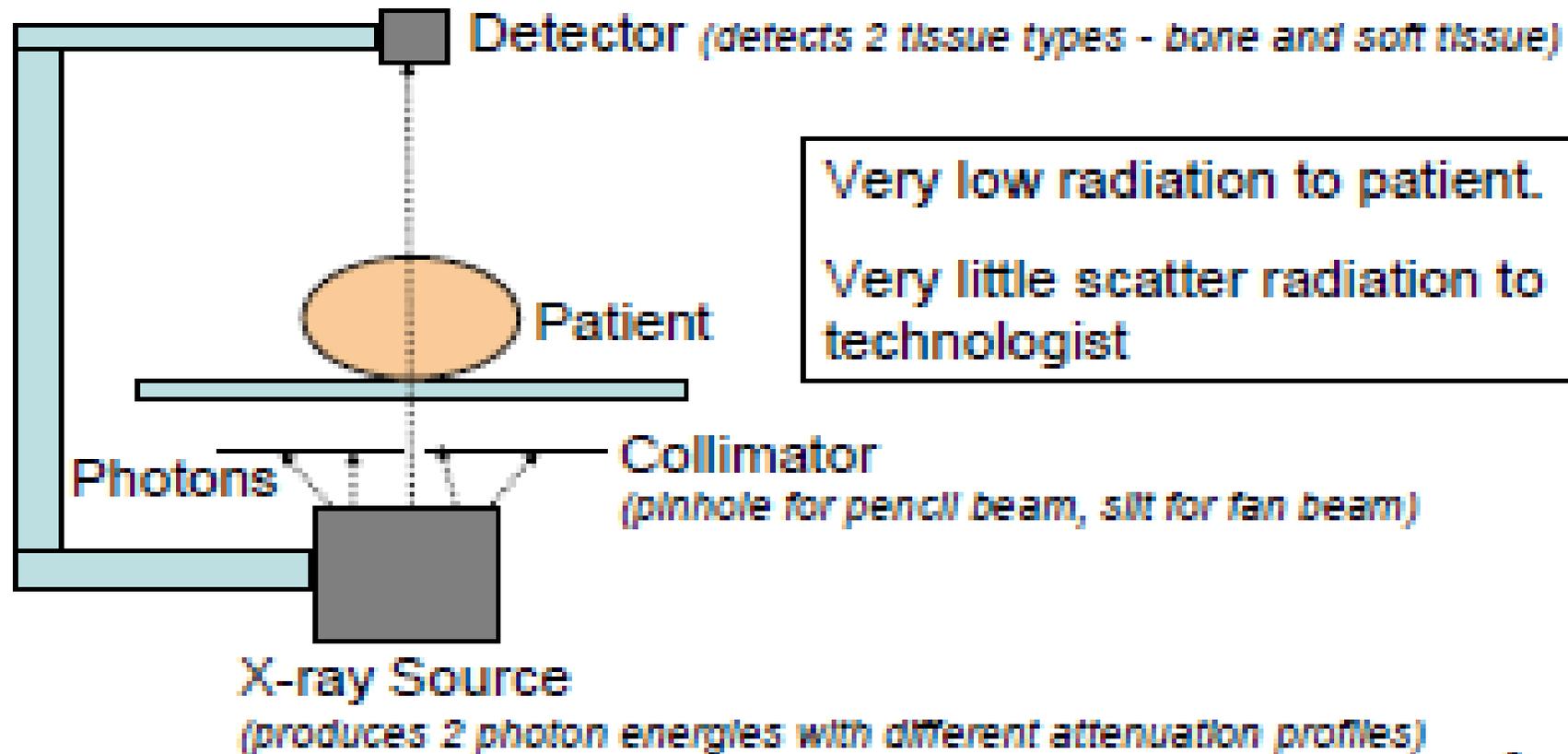
Medications that Cause Secondary Osteoporosis

- Antiepileptic drugs
- Aromatase inhibitors
- Corticosteroids
- Cyclosporine A, tacrolimus
- Depo-medroxyprogesterone
- Excessive vitamin A
- Excessive thyroxine
- Gonadotropin releasing hormone agonists
- Long-term heparin
- Lithium
- Methotrexate

Diseases Associated with Secondary Osteoporosis

- Hypogonadal status:
 - exercise-induced amenorrhea
 - anorexia nervosa and bulimia
 - premature ovarian failure
 - Hyperprolactinemia
 - Panhypopituitarism
- Other endocrine:
 - Hyperparathyroidism
 - Hyperthyroidism
 - Cushing's syndrome
- Gastrointestinal:
 - subtotal gastrectomy
 - intestinal bypass
 - inflammatory bowel disease
 - malabsorption syndromes
 - primary biliary cirrhosis & other cirrhosis

DXA Technology



Who Should Have a DXA Scan

- Women 65 and older
- Men 70 and older
- Postmenopausal women less than 65 with risk factors
- Women during the menopausal transition with risk factors such as low body weight, prior fracture
- Adults who have a disease or are taking a medication associated with low bone mass
- Adults who have had a fragility fracture
- Adults being considered for pharmacologic treatment
- Adults being treated for low bone mass to monitor treatment

T Scores

T-score

$$\frac{\text{Patient's BMD} - \text{Young-Adult Mean BMD}}{1 \text{ SD of Young-Adult Mean BMD}}$$

Example:

$$\text{T-score} = \frac{0.7 \text{ g/cm}^2 - 1.0 \text{ g/cm}^2}{0.1 \text{ g/cm}^2} = -3.0$$

**Fracture Risk
Doubles with every
SD decrease in
T score**

Diagnostic Criteria for Osteoporosis

Classification	T-score
Normal	-1.0 or greater
Osteopenia	Between -1.0 and -2.5
Osteoporosis	-2.5 or less

A presumptive clinical diagnosis can be made in at-risk individuals who sustain a low trauma fracture

Question 14

- A 71-year-old Caucasian woman presents for routine follow-up. Height is 5'5 and weight is 149lbs
- Her recent DXA scan shows a bone mineral density at the femoral neck of 0.721 g/cm^2 (T-score of -2.3)
- The patient has no history of falls, fractures, or rheumatoid arthritis, and she has never been treated with steroids. She is a former cigarette smoker, quit 12 years ago. She drinks one glass of wine with dinner, and exercises by walking 3-4 times a week. Her mother fell and fractured her hip at age 74.
- The patient recently began taking calcium 1000 mg daily and vitamin D3 800 IU daily

Question 14

In addition to continuing calcium and vitamin D, which of the following is the most appropriate recommendation for managing this patient's condition?

- A. Repeat DXA scan in 2 years
- B. Start treatment with nasal calcitonin
- C. Start treatment with oral alendronate
- D. Start treatment with denosumab
- E. Start treatment with teriparatide

Treatment of Osteoporosis

- 1st Rule out Secondary causes
- Calcium, Vitamin D and Weight-bearing
 - ~1200mg oral calcium daily for men and women >50 (**preferably through diet rather than supplements**)
 - ~800-1000 IU Vitamin D daily for men and women >50
- Indications for pharmacotherapy
 - Osteoporosis by T score (≤ -2.5)
 - If already had an osteoporotic fracture
 - At high risk for osteoporotic fracture (FRAX SCORE 10 year fracture risk >3% at hip or >20% for all fractures)
 - Chronic steroid use

Calculation Tool

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

Country: **US (Caucasian)** Name/ID: [About the risk factors](#)

Questionnaire:

1. Age (between 40 and 90 years) or Date of Birth

Age:

Date of Birth:

Y: M: D:

2. Sex

Male Female

3. Weight (kg)

4. Height (cm)

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 3 or more units/day

No Yes

12. Femoral neck BMD (g/cm²)

T-score: -2.3

BMI: 24.8

The ten year probability of fracture (%)



with BMD

Major osteoporotic

23

Hip Fracture

8.3

If you have a TBS value, click here:



Weight Conversion

Pounds kg

Height Conversion

Inches cm

04463441

Individuals with fracture risk assessed since 1st June 2011

Question 15

- A 53-year-old Caucasian female with no significant PMH comes in for her annual exam. She reports that over the past year she has had only 2 periods and has noted some fatigue and decreased libido. She reports hot flashes which occur 2-3 times daily and more frequently at night making it difficult to sleep. Her mother had osteoporosis with a hip fracture at age 71 and there is no family history of breast cancer.
- On exam BP is 120/80 HR 76 and BMI 27.2. The rest of the exam is unremarkable
- Fasting lipid panel shows total cholesterol 220 triglycerides 118 LDL 160 HDL 42

Question 15

Which of the following would be an indication for estrogen replacement therapy (HRT) in this patient?

- A. Prevention of breast cancer
- B. Treatment for vasomotor symptoms
- C. Prevention of osteoporosis
- D. Treatment of hyperlipidemia
- E. Prevention of cardiovascular disease

Treatment of Osteoporosis

- **Bisphosphonates** (pamidronate, alendronate, ibandronate, risedronate, zoledronic acid)
 - Inhibits osteoclast bone resorption
 - Side effects:
 - Osteonecrosis of the jaw- RARE
 - Oral bisphosphonates: Nausea, GERD, gastritis, esophagitis
 - Atypical Fractures – RARE
- **Denosumab**
 - Inhibits osteoclast bone resorption (monoclonal antibody to RANKL)
 - Q6 month injections
 - Safe to use in CKD
 - Side effects:
 - Increased risk of infections
 - Rashes
 - Osteonecrosis of the jaw- RARE
 - Atypical Fractures – RARE

Treatment of Osteoporosis

- Raloxifene
 - Selective Estrogen Receptor Modulator
 - Acts like estrogen on bone and anti-estrogen on breast and uterus
 - Side effects: hot flashes and blood clots
- Teriparatide (PTH 1-34) & Abaloparatide (PTHrP 1-34)
 - Stimulates bone formation
 - Daily Injection for severe osteoporosis x 2 years followed by anti-resorptive drug
 - Osteosarcoma risk

Treatment of Osteoporosis

- Romosozumab
 - Sclerostin inhibitor
 - Increases bone formation and blocks bone resorption
 - Monthly injections x 1 year then followed by anti-resorptive
 - Black Box Warning: heart attack, stroke, CV death
- Drug Holidays
 - 5 years after PO bisphosphonates
 - 3 years after IV bisphosphonates
 - No holiday after denosumab! Risk bone loss if stop >6-9 months
 - Restart if fracture occurs or BMD decreases

Paget's Disease of the Bone - AKA Osteitis Deformans

Excessive breakdown and re-growth of bones

- Diagnosis
 - Elevated alkaline phosphatase
 - X-ray with areas of resorption and formation
 - Bone Scan lights up affected areas
- Symptoms:
 - Enlargement of Bones (increased ring size, hat size)
 - Pain and warmth over affected bone
 - Nerve Compression by growing bones
 - Headaches
 - Hearing loss
 - Sciatica

Treatment of Paget's Disease

- Indications for treatment
 - Bone Pain
 - Hypercalcemia
 - Skull Involvement
 - Vertebral Involvement
 - Long bone involvement
 - Fracture
- Treat with Bisphosphonates
 - Different dosing than osteoporosis



Thank You

Next in the Series

April 28, 2021