

# Calcium and Metabolic Bone Disease

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**Special Thanks to : Ricardo Correa, M.D.**

# Objectives

Calcium distribution and homeostasis

Hyper and hypocalcemia

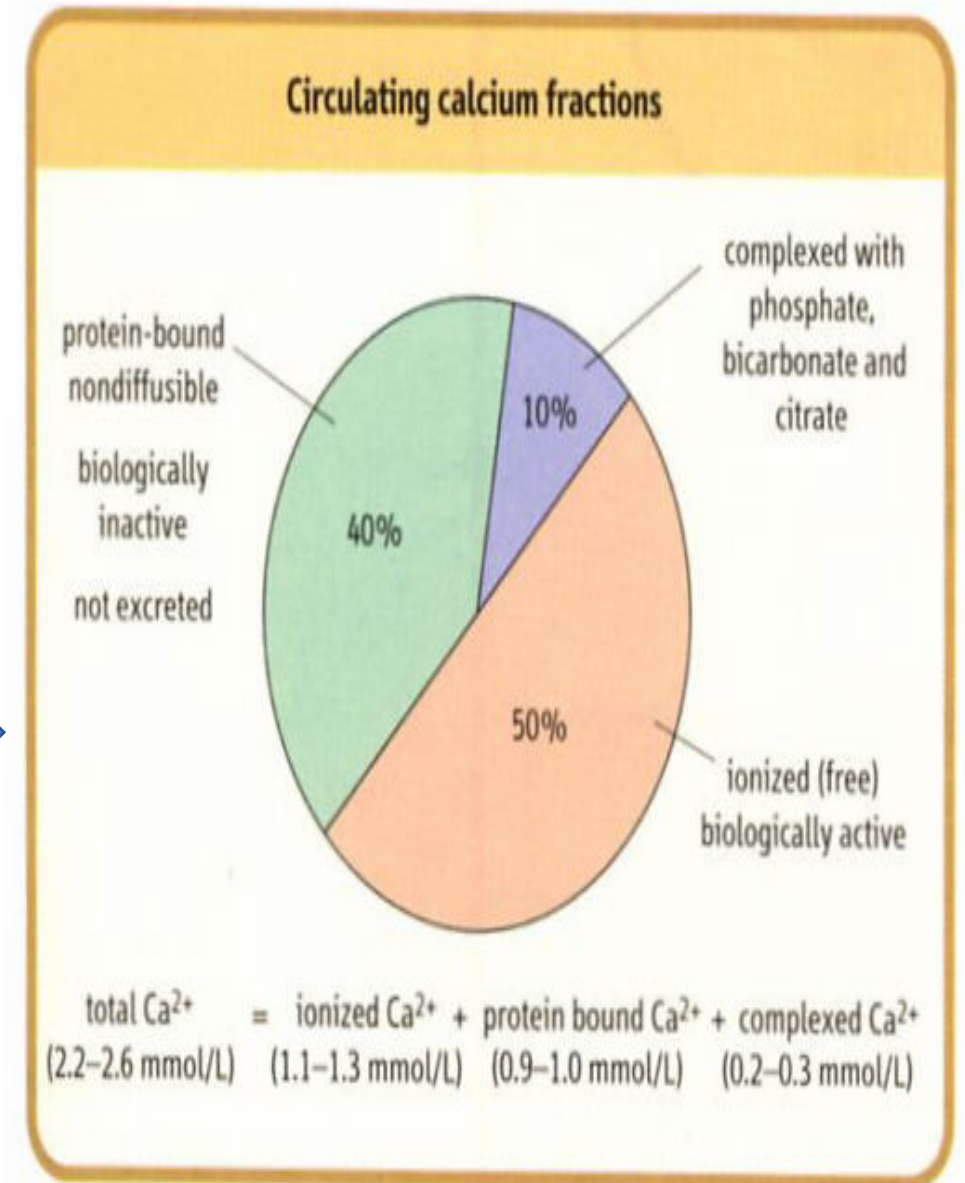
Osteoporosis

# Calcium (Ca<sup>2+</sup>)

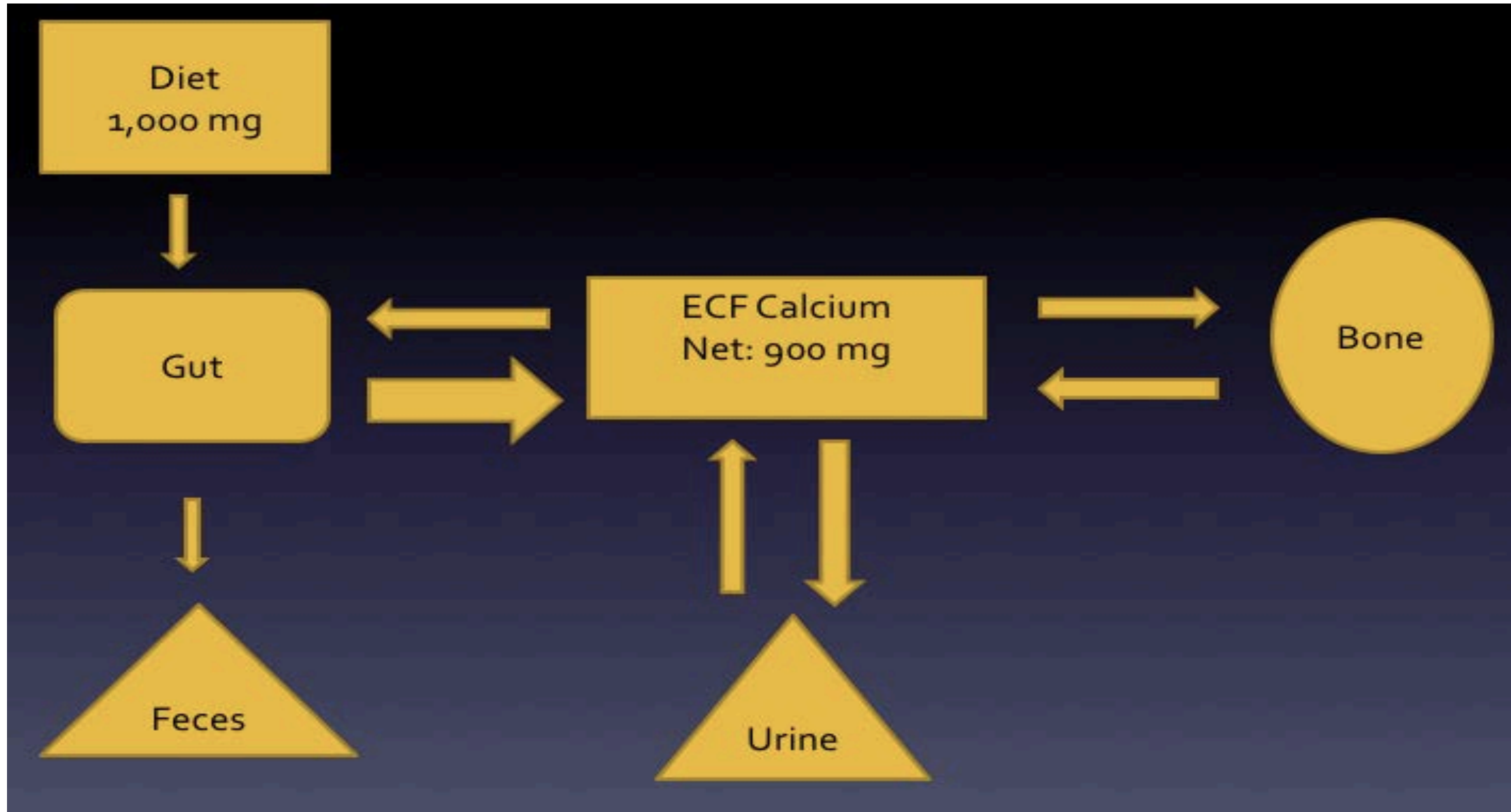
- Involved in :
  - Excitation- contraction coupling in various muscles, including the heart
  - Synaptic transmission
  - Platelet aggregation and coagulation
  - Secretion of other hormones via acting as secondary messengers
  - Bone rigidity and mineralization
  - Cell division

# Distribution in the Body

- Total body Ca content in adults is about 1000 g
  - 98-99% exists as the hydroxyapatite  $(OH)_2$  crystal in the mineral phase of bone.
  - 1-2% is found in soft tissue and the extracellular fluid (ECF) space including blood.
- Plasma proteins bound: mainly albumin (40%)
- 10 % bound with phosphate, sulphate & citrate
- About 50 % free ionized state



# Calcium Fluxes



# Serum Calcium

- Level maintained within very narrow range (**8.5-10.5 mg/dl**): measures bound to albumin
- Corrected for hypoalbuminemia: a decrease in calcium of 0.8 mg/dL for every 1 g/dL decrease in albumin

**Corrected Ca =**

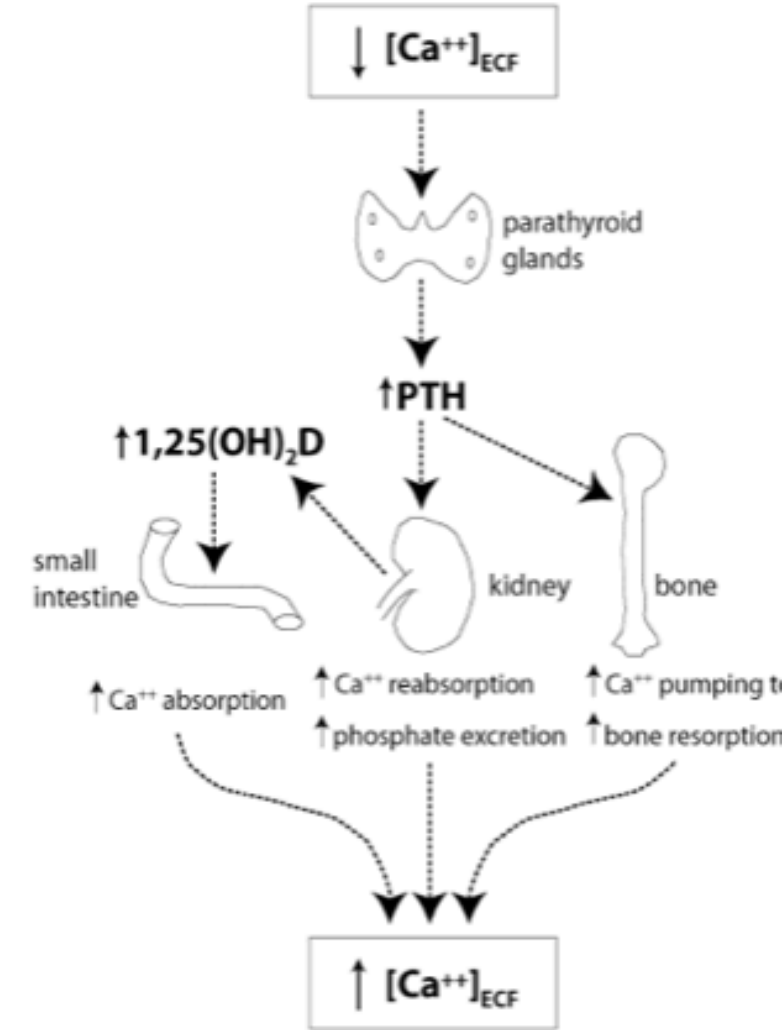
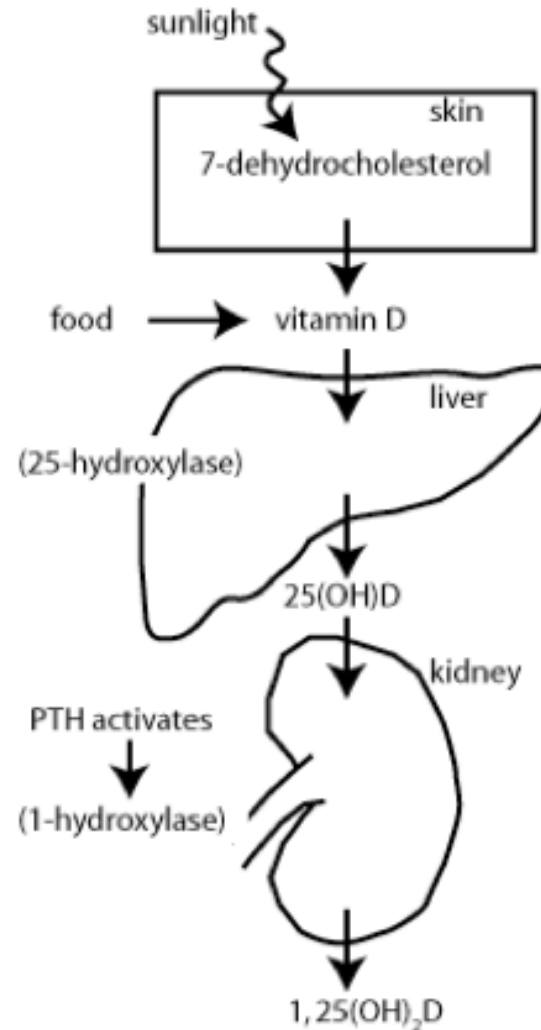
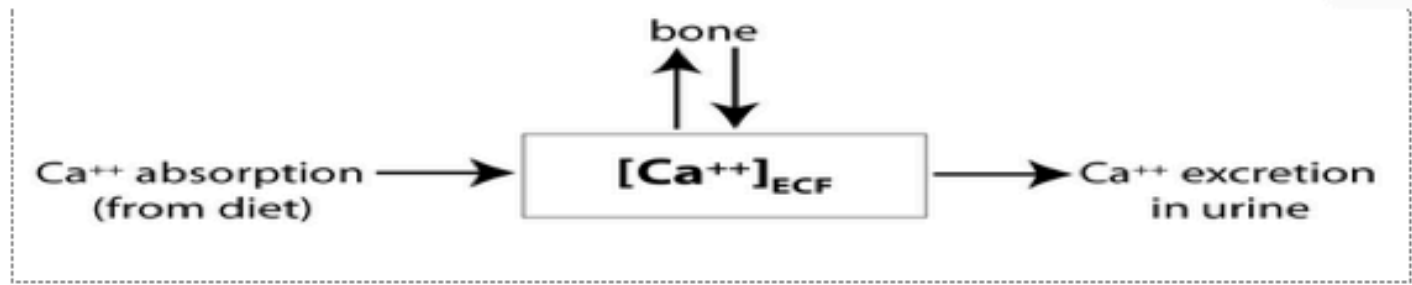
**Serum calcium + [ (4 –albumin) x 0.8]**

- Blood pH can alter the equilibrium constant of the albumin-calcium complex
  - Acidosis: decrease binding
  - Alkalosis: enhances binding

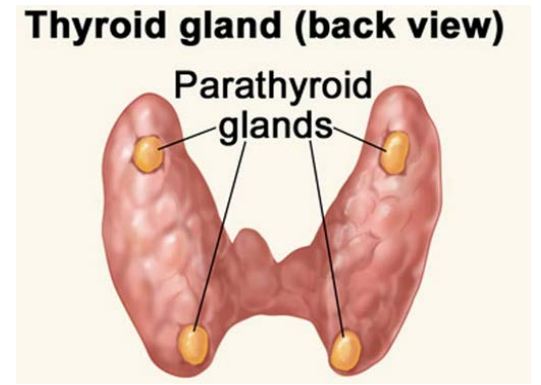
- **When to check iCa:**
  - Hyper/hypoalbuminuria
    - eg. multiple myeloma, liver disease, malnutrition, athletes on high protein diet
  - Hyperparathyroidism
    - PTH may decrease the binding of calcium to albumin and therefore increase ionized calcium at the expense of the protein-bound fraction
  - CKD (GFR <60 ml/min) with low bicarbonate/albumin
    - the total serum calcium concentration is not reliable, even if corrected for a low serum albumin

# Calcium homeostasis

- **s/Ca Regulated by: PTH, VIT D, Ca ion itself and PO4**
- PTH and Vit D regulate Ca via effects on bone, kidney, and GIT
- Ca itself regulates its own blood levels
  - Acting via CaSR in parathyroid gland to inhibit PTH secretion
  - CaSR in loop of henle: stimulate renal Ca excretion



# Parathyroid hormone



- **Secreted** by 4 parathyroid glands (12-15% population have 5<sup>th</sup> gland)
- Provides minute - minute regulation of serum ionized Ca
- Also involved in PO<sub>4</sub> homeostasis
- **Ca homeostasis** by PTH: 3 principal target organs:
  - **Bone:** increase osteoclastic activity → bone resorption → ↑s/Ca
  - **Intestinal Mucosa (indirect effect):** via ↑renal production of 1,25 OH D → ↑Intestinal Ca absorption in small intestine
  - **Kidney:** ↓Urinary Ca excretion → stimulate Ca reabsorption in distal tubule
- **Regulated** by: - f.b from s/Ca → sense iCa in parathyroid cells by CaSR
  - Low iCa<sup>2+</sup> : stimulates PTH release
  - High iCa<sup>2+</sup> : inhibits PTH release

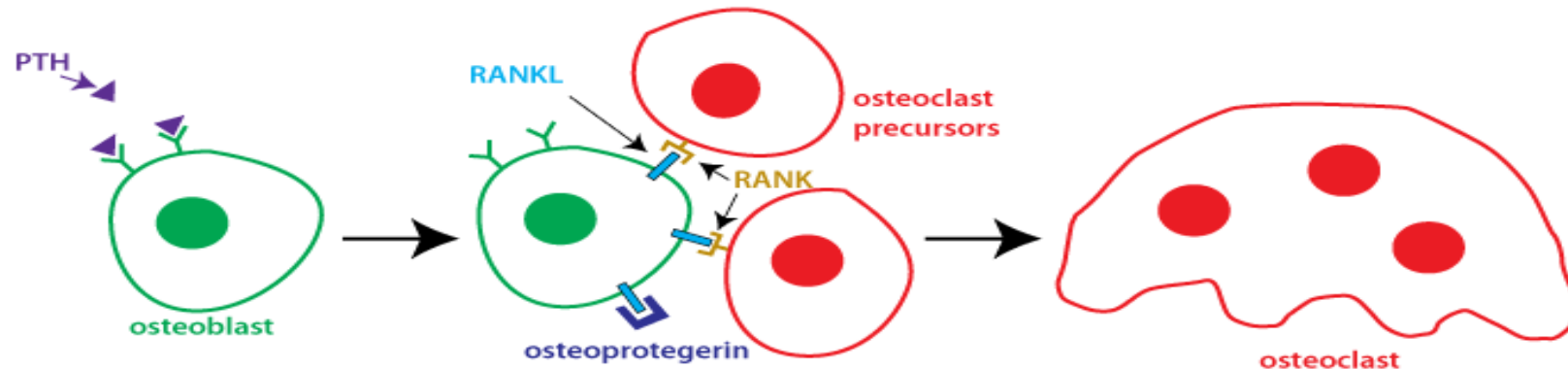


# Normal Bone Physiology

- Bone is composed of tough organic matrix that is strengthened by deposits of calcium salts.
  - The major crystalline salt is hydroxyapatite
    - Comprised of calcium and phosphate
- **3 major cells** involved in bone remodeling
  - **Osteoblasts** – “bone forming” cells that can differentiate into osteoclasts
  - **Osteocytes**- are bone cells that make type 1 collagen
  - **Osteoclasts** - “bone resorbing” cells

# PTH & Bone Resorption

- PTH acts **indirectly** to **↑ osteoclast formation**.
- It binds to osteoblasts → increased expression of RANK-L → binds to the RANK-L receptor on osteoclast precursors → increase in osteoclasts
- Osteoclasts bind to the bone surface and cause demineralization of the bone → breakdown of hydroxyapatite → **↑ in Ca & PO<sub>4</sub>**

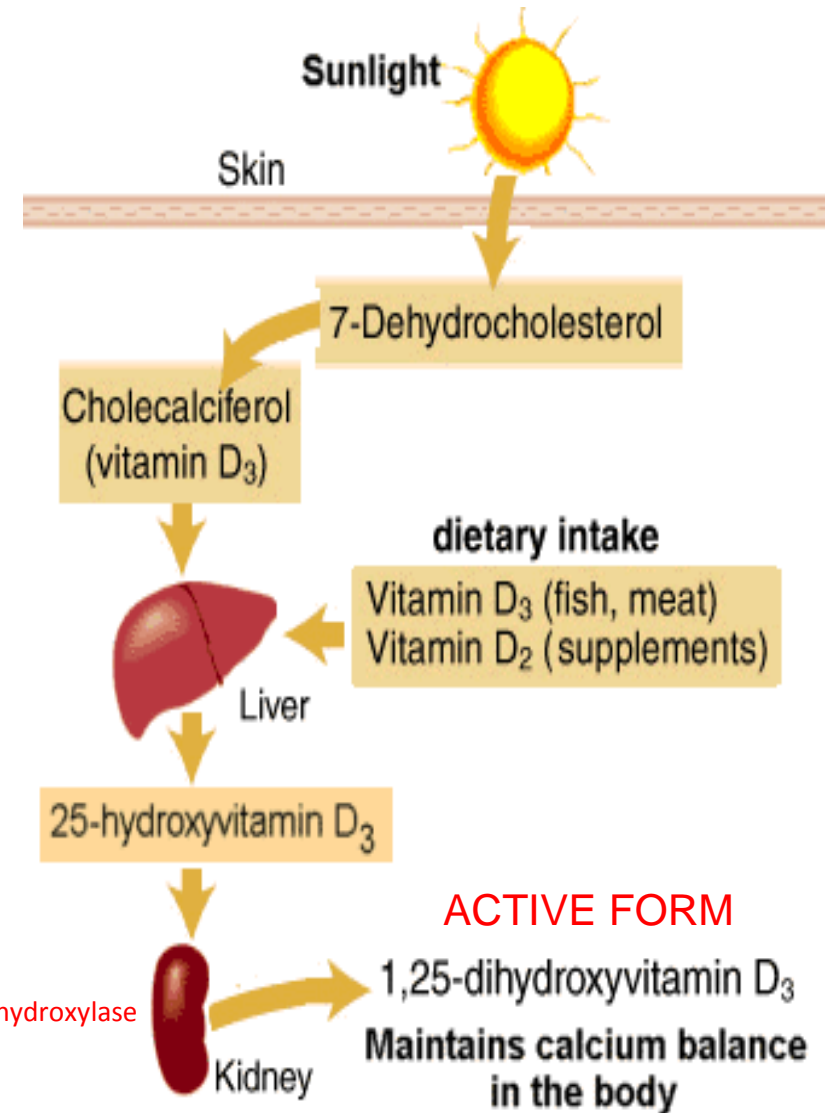


# PTH and Renal Tubules

- Has direct effects on tubular reabsorption of Ca & PO<sub>4</sub>
  - **Increases** reabsorption of **calcium** in the distal convoluted tubule
  - **Inhibits** reabsorption of **phosphate** in the proximal tubule
  - Stimulates **synthesis of 1-alpha hydroxylase** in the proximal tubules (catalyzes calcidiol → calcitriol)
  - **Decreases** activity of **24-hydroxylase** (which would normally inactivate calcitriol)

# Vitamin D

- Prohormone that regulates Ca and PO<sub>4</sub> homeostasis
- Major forms (inactive)
  - D<sub>2</sub> – Ergocalciferol (plants, yeast)
  - D<sub>3</sub> – Cholecalciferol (UV rays, animal skin)
- **Actions of Vit D active form (1,25 OHD)**
  - **Gut:** ↑ Intestinal Ca & PO<sub>4</sub> absorption
  - **Bone:** Important in bone formation & resorption
  - **Kidney:** ↑ Ca & PO<sub>4</sub> reabsorption
  - inhibits the synthesis and secretion of PTH, providing -f.b regulation of 1,25-dihydroxyvitamin D (calcitriol) production.



# Calcitonin

- Hormone secreted by parafollicular C cells of the thyroid
  - Increases in response to hypercalcemia
  - Secretion is inhibited in response to hypocalcemia
- **Main action**
  - Inhibits osteoclast-mediated bone resorption → **↓ in serum calcium and phosphate**
  - **↓** renal tubular reabsorption of calcium and phosphate
  - **↓** gut absorption of phosphate

# Summary of Net Effects

## ⦿ PTH

- ↑ calcium
- ↓ phosphate

## ⦿ Calcitriol (**Active Vitamin D**)

- ↑ calcium
- ↑ phosphate

## ⦿ Calcitonin

- ↓ calcium
- ↓ phosphate

# Optimal Ca & Vit D

- Vitamin D
  - ~ 600-800 IU daily
    - no consensus on the optimal 25(OH)D concentration for skeletal or extra-skeletal health.
    - serum 25(OH)D concentration of 20 ng/mL (50 nmol/L) is sufficient for most individuals
- Calcium
  - 1,000-1,200 mg elemental calcium daily

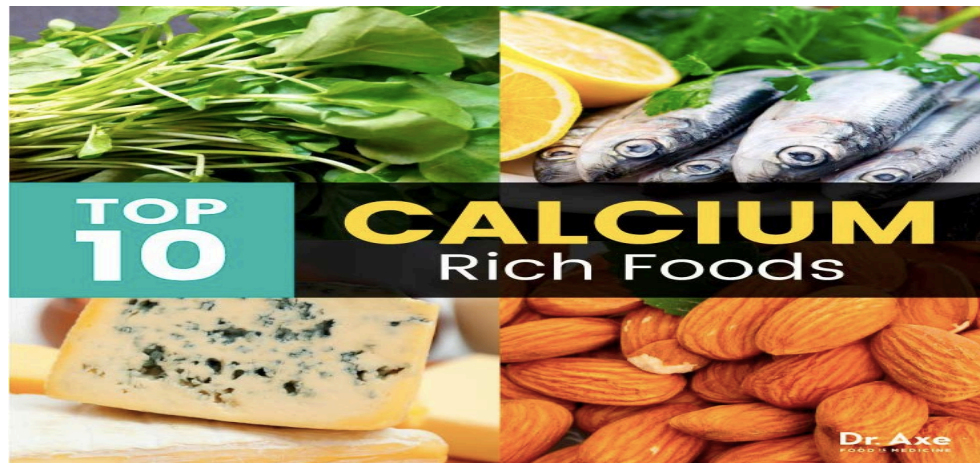
# Sources of Vitamin D

Food	Serving Size	International Units of Vitamin D
Cod Liver Oil	One tablespoon	1360
Swordfish	Three ounces	566
Salmon	Three ounces	477
Canned Tuna in Water	Three ounces	154
Orange Juice with Vitamin D	One cup	137
Milk with Vitamin D	One cup	115-124
Yogurt with Vitamin D	Six Ounces	80
Cooked Beef Liver	Three ounces	42
Eggs (Yolk)	One	41



# Sources of Calcium

Compound	Brand Name	Compound Content (mg)	% Ca	Elemental Ca (mg)
Calcium Acetate	Phoslo™	667	25%	167
Calcium Carbonate	Chooz™ (Gum)	500	40%	200
	TUMS™			
	TUMS EX™	750	40%	300
	TUMS Ultra™	1,000	40%	400
	LiquiCal	1,200	40%	480
	CalciChew™	1,250	40%	500
	CalciMix™			
	Oscal 500™			
	TUMS 500™			
Caltrate 600™		1,500	40%	600
NephroCalci™				
Calcium Citrate	CitraCal™			
Calcium Acetate + Magnesium Carbonate	MagneBind™ 200	200 Mg carbonate		(Mg = 57 mg)
		450 Ca acetate		113 mg
Calcium Carbonate	MagneBind™	300 Mg carbonate		(Mg = 85 mg)
		300 Ca acetate		76 mg



<https://draxe.com/top-10-calcium-rich-foods/>

## Top 10 Calcium Rich Foods

### 1) Raw Milk

1 cup: 300 mg (30% DV)

### 2) Kale (cooked)

1 cup: 245 mg (24% DV)

### 3) Sardines (with bones)

2 ounces: 217 mg (21% DV)

### 4) Yogurt or Kefir

6 oz: 300 mg (30% DV)

### 5) Broccoli

1 ½ cup cooked: 93 mg (9% DV)

### 6) Watercress

1 cup: 41 mg (4% DV)

### 7) Cheese

1 oz: 224 mg (22% DV)

### 8) Bok Choy

1 cup: 74 mg (7% DV)

### 9) Okra

1 cup: 82 mg (8% DV)

### 10) Almonds

1 oz: 76 mg (8% DV)

# Hypercalcemia

# Definition

- **Normal** serum calcium: **8.5 to 10.5** mg/dl
- **Mild** hypercalcemia: **>10.5 but  $\leq$  12** mg/dl
- **Moderate** hypercalcemia: **>12 but  $\leq$  14** mg/dl
- **Severe** hypercalcemia: **>14** mg/dl

# Etiologies

## PTH Dependent

- Primary hyperparathyroidism
- Familial Hypocalciuric Hypercalcemia
- Lithium Toxicity
- Tertiary Hyperparathyroidism

## PTH Independent

- Hypercalcemia of malignancy
  - Local osteolytic
  - Humoral hypercalcemia of malignancy
- Granulomatous disease
- Hyperthyroidism/ Thyrotoxicosis
- Adrenal Insufficiency
- Thiazide diuretics
- Vitamin D & Vitamin A intoxication
- Milk Alkali Syndrome (intake of >5 g Ca/day)
- Immobilization
- Renal Failure
  - ARF
  - CRF with aplastic bone disease

# Clinical manifestations

*“stones, bones, groans, psychiatric overtones”*

- “Stones”: Kidney stones
- “Bones”: Bone pain, osteoporosis, fractures, loss of height, deformities
- “Groans”: Muscle weakness, N/V/abdominal pain, constipation, polyuria, polydipsia
- “Psychiatric overtones”: Anxiety, depression, cognitive dysfunction, lethargy
- In addition: Renal insufficiency, pancreatitis, cardiac arrhythmias

# Variety of Clinical Presentation

- **Mild Hypercalcemia:** calcium  $<12$  mg/dL
  - Asymptomatic or nonspecific symptoms: constipation, fatigue, depression
- **Moderate Hypercalcemia:** calcium 12-14 mg/dL
  - Tolerated well chronically
  - Acute elevations  $\rightarrow$  polyuria, polydipsia, dehydration, anorexia, and changes in mental status
- **Severe Hypercalcemia:** calcium  $>14$  mg/dL
  - Worsening of symptoms

# Approach to hypercalcemic patient

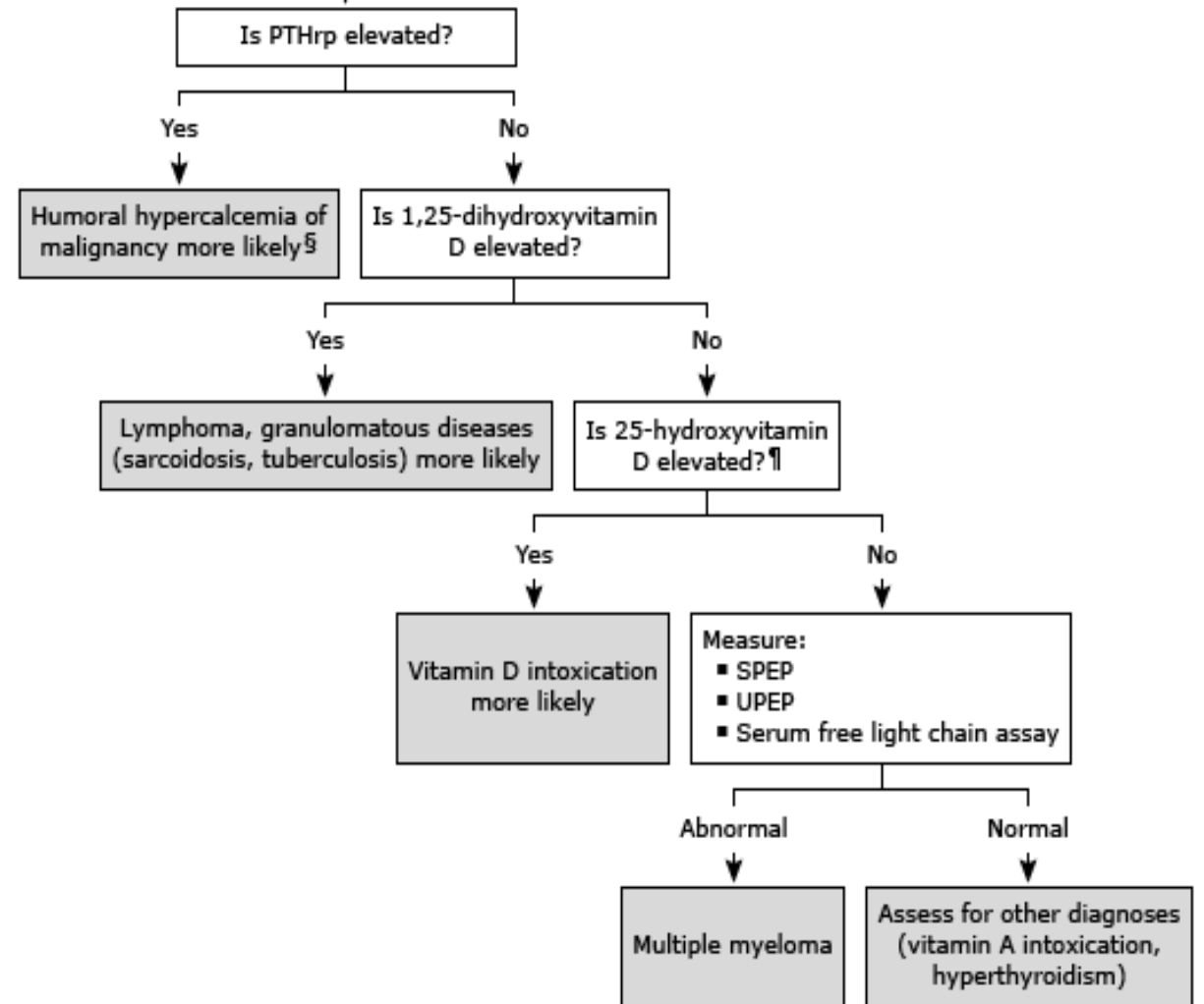
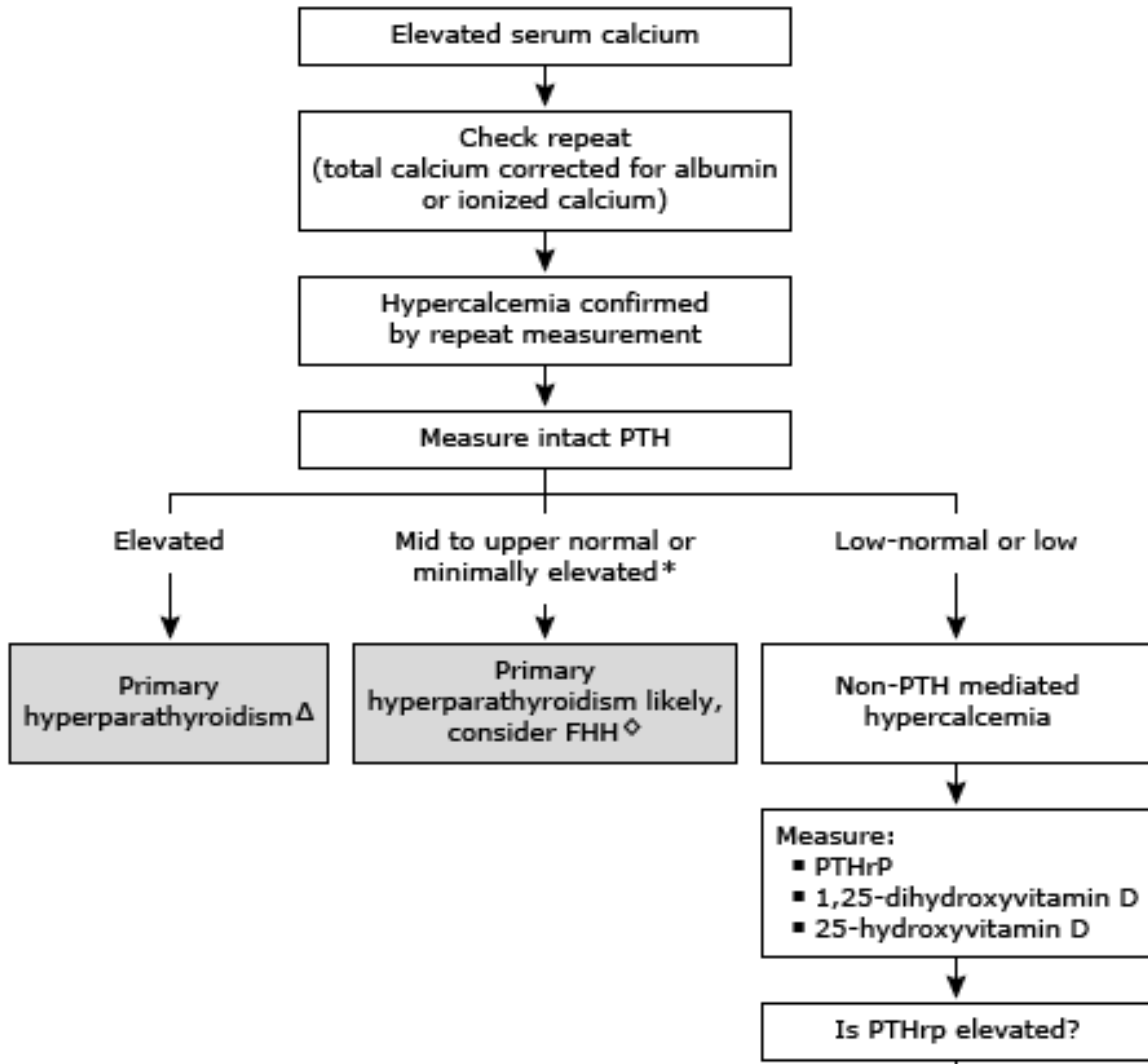
- First, distinguish hemoconcentration or rare Ca-binding paraproteinemia or thrombocythemia-associated hypercalcemia (release of intracellular Ca in vitro) from a true increase in s/ iCa-> measure iCa, repeat total Ca with albumin
- Always differentiate between **PTH mediated** and **non PTH mediated**
- **Most common:** Primary Hyperparathyroidism
  - **Out patient : More than 90 % cases** hypercalcemia
  - Mild, stable, or long duration hypercalcemia but otherwise healthy
- **Ill/ hospitalized patients: 50 % malignant** hypercalcemia
  - Evidence of malignant disease

# Initial Workup

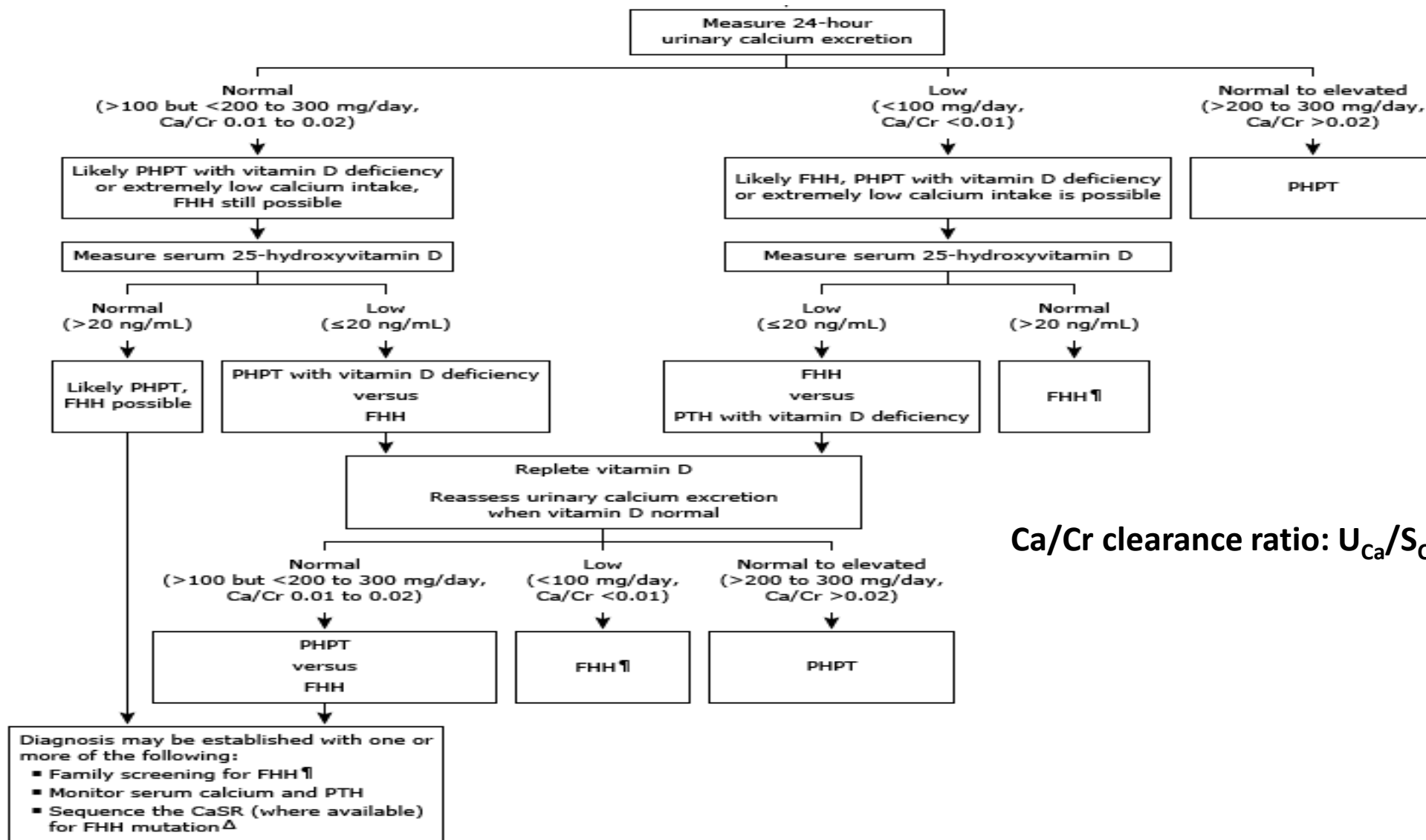
- H & P (kidney stones, fractures, weight loss, PUD, back/bone pain, medications, FHx)
- Compare previous labs -> ? Chronicity
- Labs: Electrolytes, BUN, Cr, PO<sub>4</sub>, ALP, 25-OH Vit D, s/albumin, s/Ca, iCa (if applicable), PTH
- PTH-> caution can be inappropriately normal
- EKG – look for short QT, prolonged PR



# Work up algorithm



# PTH Dependent Hypercalcemia work up: PHPT Vs FHH



$$\text{Ca/Cr clearance ratio: } U_{\text{Ca}}/S_{\text{Ca}} \times S_{\text{Creat}}/U_{\text{Creat}}$$

# Treatment

- **Supportive measures:**

- Aggressive IVF: isotonic initial rate of 200-300 ml/h; then adjusted to maintain UOP at 100-150 ml/h
  - Careful with CHF or Renal Failure: can use loop diuretics
- Telemetry: short QT, prolong PR

- **Medical Therapy:**

- Calcitonin
- Bisphosphonates
- Denosumab
- Steroids

# Calcitonin

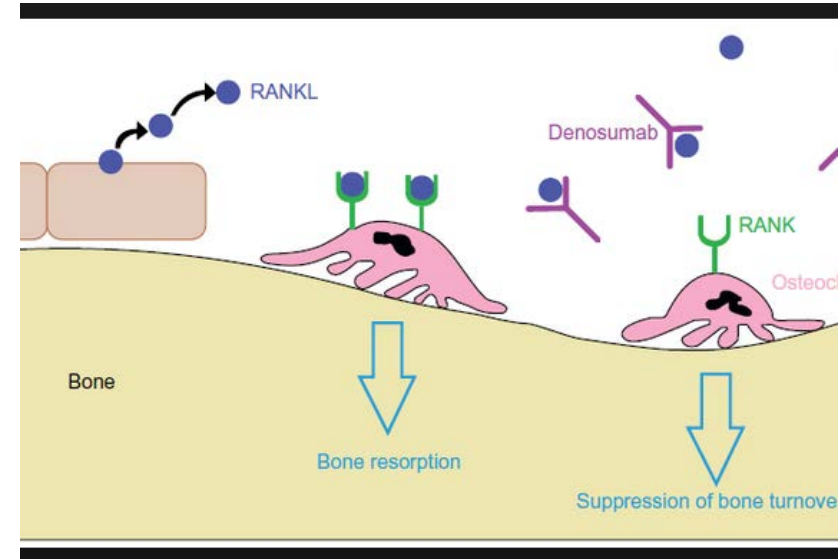
- Inhibits osteoclast resorption of bone and increases renal excretion of calcium and phosphate
- Usually used as a bridge to bisphosphonates
- **Benefit**- works quickly
  - Lowers serum calcium by 1- 2 mg/dL within four to six hour
- **Con**- effect wanes after 48 hours (tachyphylaxis)
- **Dose**: Initial: IM or SubQ: 4 units/kg every 12 hours; may increase up to 8 units/kg every 6 to 12 hours
- **S/E**: generally well tolerated; only transient N/V, abdominal cramps, flushing, & local skin rxn

# Bisphosphonates

- **Drug of choice:** inhibit bone resorption
  - s/Ca usually decline within 24 h; lowest in a week after single infusion
  - Duration of response: 1-2 wks to several months
- **FDA approved:** Pamidronate and Zoledronate
  - ZA: 4 mg IV over 15 minutes (preferred: more potent)
  - PA: IV 60 to 90 mg over two hours
- Don't use in Milk Alkali Syndrome: induce postRx Hypocalcemia
- **Caution** with renal Failure (C/I: GFR < 30 ml/min)
- **S/E:** local pain or swelling at the infusion site, flu-like symptoms, transient lymphopenia, mild hypophosphatemia or hypomagnesemia, hypocalcemia, ONJ

# Denosumab

- Monoclonal Ab to RANK-L → inhibits Osteoclasts
- For malignancy associated or bisphosphonate refractory hypercalcemia
- Alternative for renal failure
- Dosing: 60 mg SQ weekly for 4 wks and then 60 mg/month
- Small risk of ONJ



# Glucocorticoids

- Used in patients where hypercalcemia is NOT d/t increased bone resorption. (Vit D dependent Hypercalcemia)
  - Excessive Ca intake
  - Vit D toxicity
  - Chronic Granulomatous diseases e.g Sarcoidosis, Lymphoma etc
    - Granulomas have 1-alpha hydroxylase so increase production of calcitriol
- MOA: decrease calcitriol production in mononuclear cells in lungs and lymph nodes
- IV or oral; oral dose usually 20-40 mg/day
- Takes 2-5 days to act

# Other options

- **Dialysis:** last resort
  - Severe renal insufficient, with or without complicating heart dz
- **Calcimimetic:** Cinacalcet
  - Mimics axn of Ca on tissues → increased sensitization of CaSR
  - May be effective in some patients with parathyroid cancer



# Hypocalcemia

# Definition

- Serum Ca **below lower limit of normal**
- Common cutoffs:
  - Adults: total Ca < 8.4 mg/dl; iCa: < 4.4 mg/dl
  - Children: total Ca < 8.5 mg/dl; < 7 mg/dl in preterm infant; iCa < 4 mg/dl

# Pseudohypocalcemia

- **Hypoalbuminemia**

- Total calcium may vary but iCa remains stable
- e.g Volume overload, malnutrition, nephrotic syndrome, chronic illness

- **Acid base disorders:** although albumin level may be normal, change in blood pH can alter equilibrium constant of albumin-Ca complex

- Acidosis: decreased binding of albumin-calcium
- Alkalosis: increased binding of albumin-calcium
- e.g: critically ill or post surgical patients
- Check iCa

# Etiologies

## Low PTH (Hypoparathyroidism)

- Genetic disorders
  - Abnormal parathyroid gland development
  - Abnormal PTH synthesis
  - Activating mutation of CASR (normal or low PTH)
- Postsurgical (thyroidectomy, parathyroidectomy, radical neck dissection)
- Autoimmune
  - APS syndrome type I or isolated hypopara d/t activating AB to CASR
- Radiation destruction
- Infiltrative dz
- Hungry bone syndrome (post-parathyroidectomy)
- HIV infection

## High PTH (secondary hyperpara in response to hypocalcemia)

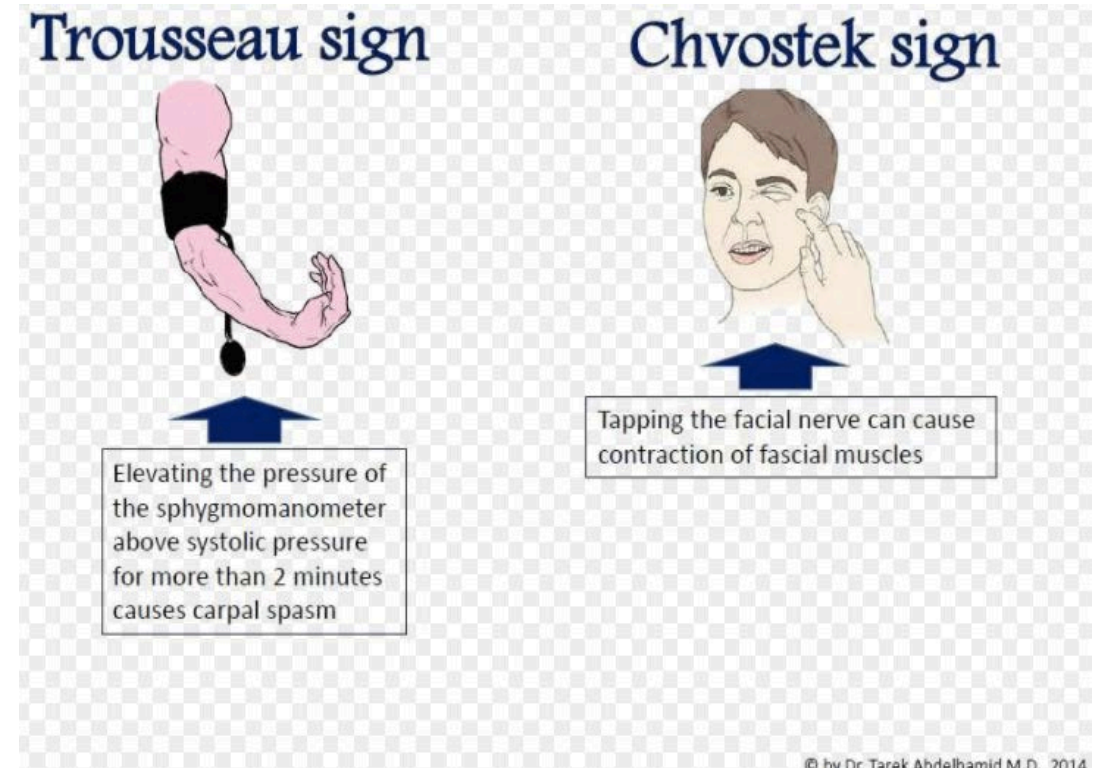
- Vit D deficiency or resistance
- PTH resistance
  - Missense mutation in PTH
  - Pseudohypoparathyroidism
  - Hypomagnesemia
- Renal disease
- Loss of Calcium from circulation
  - Hyperphosphatemia
  - Tumor lysis syndrome
  - Acute pancreatitis
  - Osteoblastic metastasis
  - Acute respiratory alkalosis
  - Sepsis or acute severe illness

**Drugs:** Bisphosphonates, calcitonin, denosumab (esp with Vit D deficiency); Cinacalcet; Ca chelators (EDTA, citrate, Phosphate); Foscarnet, phenytoin, fluoride poisoning

# Clinical Presentation

- Mild cases: asymptomatic
- Classic Symptoms → Neuromuscular irritability: perioral paresthesias, tingling of fingers and toes, tetany
- Severe cases: prolonged QT, arrhythmias, seizures, laryngospasm

## Exam findings



**Chronic cases:** dry scaly skin, coarse brittle hair, chronic pruritis  
Cataracts, delayed tooth eruption, hypoplastic tooth enamel  
Edema  
Short 4<sup>th</sup> or 5<sup>th</sup> metacarpals (Albright Hereditary Osteodystrophy)

# Diagnosis

- Confirm Hypocalcemia: **repeat labs** → total Ca with albumin or iCa

**Corrected Ca = Serum calcium + [ (4 - albumin) x 0.8]**

- History
- **Supportive labs:** PTH, PO4, BUN/Cr, Mg, Vit D (25-OHD & 1,25-OHD), ALP

	Normal or low PTH	High PTH
Normal or low PO4	Suspect hypomagnesemia or CASR defect	<ul style="list-style-type: none"><li>• Suspect Vit D deficiency</li><li>• If 25OHD normal: suspect end-organ resistance (Vit D dependent rickets or sclerotic bone metastases)</li></ul>
High PO4	Suspect Hypoparathyroidism	<ul style="list-style-type: none"><li>• Suspect renal dysfunction</li><li>• If normal BUN/Cr, 25-OHD &amp; ALP suspect Pseudohypoparathyroidism</li></ul>

# Additional Testing

- Elevated **ALP**: Osteomalacia 2/2 severe Vit D def & secondary hyperparathyroidism; can occur with Osteoblastic Bone mets
- **Amylase**
- **Urine creatinine to Calcium ratio**
  - low urinary calcium with untreated hypoparathyroidism or Vit D def
  - Normal PTH with hypercalciuria: may indicate AD hypercalciuria
- **Urine creatinine to Mg ratio**: hypomagnesemia d/t renal loss
- **X-ray** of wrist or knee: rickets (cupping & fraying of metaphyses)
- **ECG**: prolonged QT, heart block
- **Genetic testing**

# Treatment

- **Acute/Symptomatic and asymptomatic with corrected Ca < 7.5 mg/dl: Urgent Rx**
  - IV Calcium bolus:
    - 10 ml of 10% Ca-gluconate in 50 ml 5% dextrose: over 10 min; repeat until symptoms resolve
  - Followed by IV infusion until patient receiving an effective regimen of oral Ca and Vit D
    - Dilute 10 amps of 10% Ca-gluconate in 1 L of D5W or NS: infusion 50 ml/h
    - Goal to achieve s/Ca at lower end of normal
  - EKG monitoring
- **Asymptomatic and Chronic Hypocalcemia:**
  - **Ca regimen: 1.5-2 gm of elemental Ca in divided doses**
    - CaCO<sub>3</sub>: taken with food, 40% elemental Ca
    - Ca-citrate: not dependent on food for absorption, ~20% elemental Ca → preferred if GI upset with CaCO<sub>3</sub> or h/o kidney stones
  - **Vit D regimen:**
    - Vit D def: ergocalciferol or cholecalciferol
    - Hypopara, pseudohypopara, or Vit D dependent rickets: calcitriol or alfacalcidol



# Other consideration for treatment

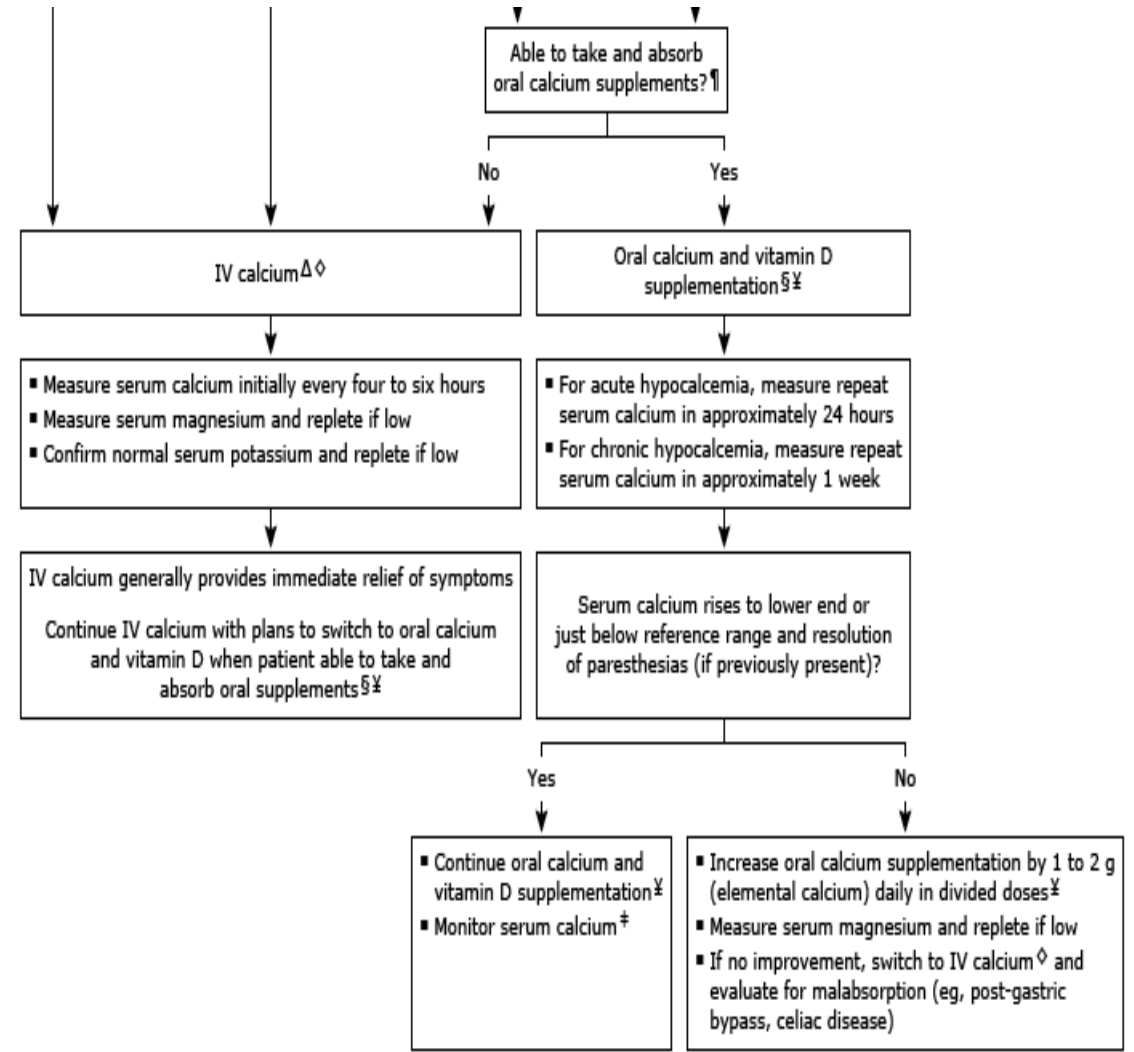
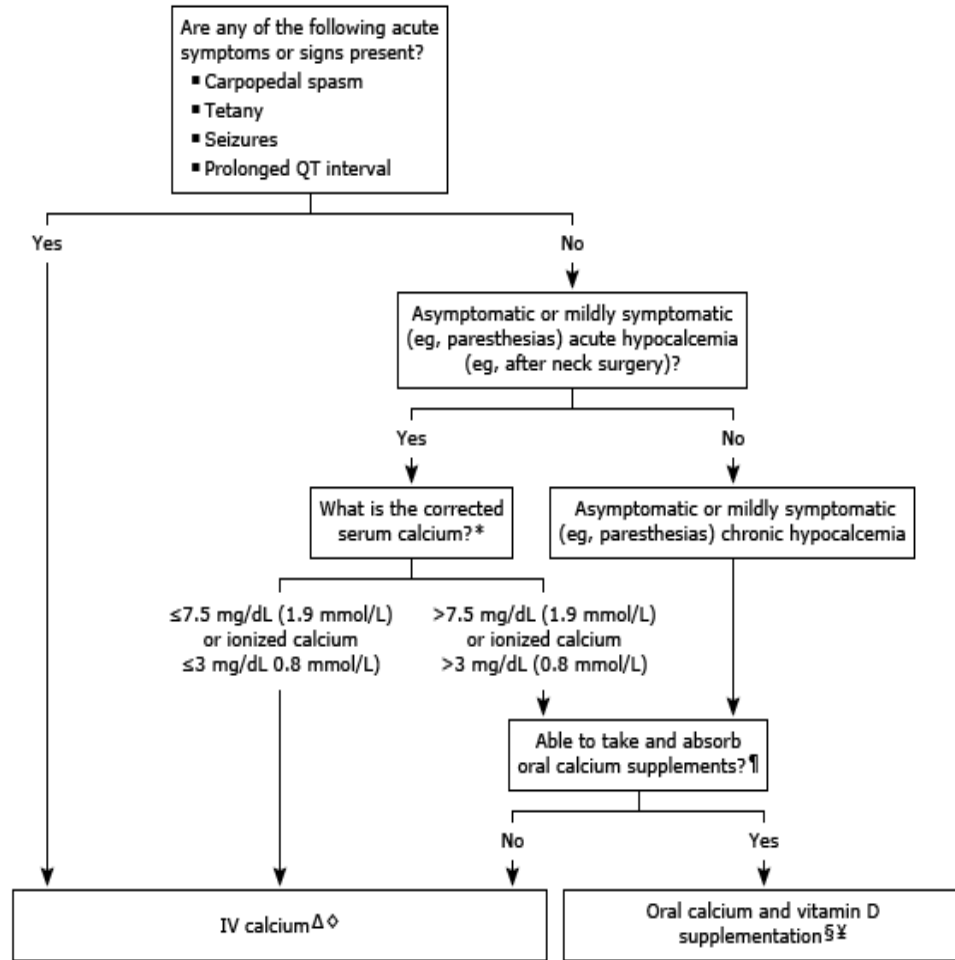
- **For Hypoparathyroidism**

- Calcitriol 0.25 to 0.5 mcg twice daily and oral Ca (1-4 g elemental CaCO<sub>3</sub> daily in divided doses)
- Correct Concurrent **Hypomagnesemia**: IV MgSO<sub>4</sub> for symptomatic Hypomagnesemia (target > 1 mg/dl); oral for asymptomatic mild – mod hypomagnesemia
- **R-PTH**: recombinant PTH for refractory chronic Hypoparathyroidism
- **Thiazide diuretics**: reduce urinary Ca-excretion by enhancing distal renal tubular reabsorption; esp in Autosomal Dominant Hypocalcemia (activating mutation of CaSR gene)

# Treatment

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## Initial management of hypocalcemia in adults without chronic kidney disease—mineral and bone disorder



# Follow up for Chronic Hypocalcemia

- Depends on underlying cause
- **Hypoparathyroidism:**
  - **Goal:** relieve symptoms and **maintain s/Ca in low-normal range**
  - Monitor levels q 3-6 months once stabilized
  - Monitor urinary calcium excretion annually & reduce Vit D dose if elevated → risk of Nephrocalcinosis with hypercalciuria

# Osteoporosis

# Definition

- Systemic skeletal disease characterized by Low bone mass, micro-architectural disruption, increased skeletal fragility, resulting in decreased bone strength and an increased risk of fracture
  - Most affected sites: hip, spine, & wrist
- Dual-energy X-ray absorptiometry (**DXA**): standard criterion for evaluation of BMD
  - **T score**: value compared with that of control subjects who are at their peak BMD
  - **Z-score**: value compared with that of persons matched for age and sex
    - Used for premenopausal women
    - Men younger than 50 y
    - Children

# Epidemiology & Pathogenesis

- Prevalence in adults aged  $\geq 50$  years in United States
  - > 10 million persons overall
  - > 33 million have low bone density at hip
- **Healthy bone:** bone resorption (osteoclast cells) is balanced by bone formation (osteoblast cells)
- **Bone loss** occurs when bone resorption outpaces bone formation
- Primary OP: a/w aging & sex steroid deficiency
- Secondary OP: bone loss from specific causes

# Risk Factors

- Aging
- Female Gender
- Postmenopausal/ Estrogen deficiency
- Caucasian or Asian race
- Thin body habitus/ low BMI
- Positive Family History
- Personal h/o fracture as an adult
- Cigarette smoking
- Excessive Alcohol consumption (  $\geq 3$  drinks/day)
- Immobility
- Low dietary calcium/Vit D, excess Vit A intake
- Malabsorption
- Chronic Inflammation & other medical conditions: RA, SLE, liver dz, DM, COPD, HIV
- Connective tissue disorders
- Endocrinopathies
- Medications: long term Steroids, Phenytoin, Phenobarbital, Li+, PPI, TZDs, long term heparin, aromatase inhibitors, Chemotherapy

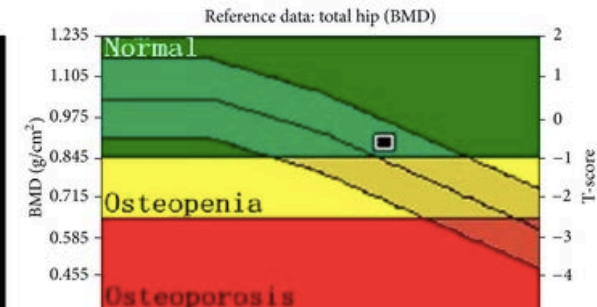
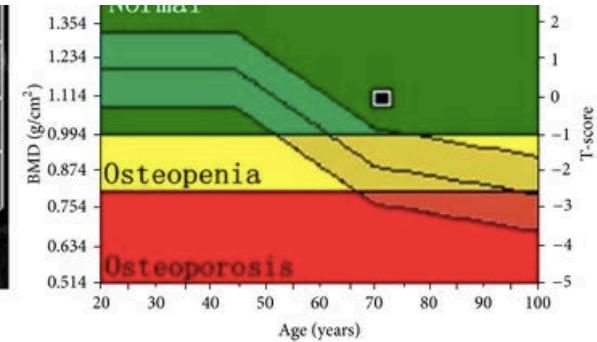
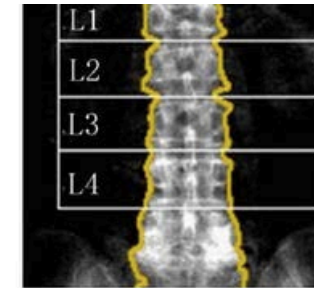
# Clinical Presentation

- Asymptomatic until fracture occurs
- Loss of height
- Acute pain followed by minor trauma
- Limited ROM
- Decreased weight bearing
- May have issues with balance
- Incidental radiographic vertebral Fx
- Fracture at certain areas most likely to be d/t OP:
  - Femoral neck fx
  - Pathologic fx of vertebrae
  - Distal radius fx
- Detected on screening



# Diagnosis based on DXA scan (WHO criteria)

- T-score:  $\geq -1$  SD considered **Normal**
- T-score:  $-1$  to  $-2.5$  SD indicates **Osteopenia**
- T-score:  $\leq -2.5$  SD indicates **Osteoporosis**
- T-score:  $\leq -2.5$  SD with **fragility fracture(s)** indicates **Severe osteoporosis**
- Z-score:  $\leq -2.0$  SD: below the expected range for age
- Z-score:  $> -2.0$  SD: within the expected range for age



# Diagnosis and Screening

- **Clinical Dx:** fragility fx regardless of any test results
- **Screening DXA scan**
  - All women  $\geq 65$  years old, and all men  $\geq 70$  years old
  - postmenopausal women  $< 65$  years old, peri-menopausal women, and men aged 50-69 years with clinical risk factors for fracture
  - any adult with fracture after age 50 years
  - any adult with condition (such as rheumatoid arthritis) or use of medication (such as glucocorticoids  $\geq 3$  months) associated with low bone mass or bone loss

# FRAX

- Clinical tool for assessment **10 year probability of hip fx or major osteoporotic fx**
- Can be used **without BMD**: based solely on risk with consideration of treatment
- **With low BMD** but not in osteoporotic range → to guide for need for therapy
- **MOF  $\geq 20\%$ , Hip fx  $\geq 3\%$**

FRAX<sup>®</sup> Fracture Risk Assessment Tool

Home Calculation Tool Paper Charts FAQ References English

## 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/cm<sup>2</sup>)  
Select BMD

### Weight Conversion

Pounds   kg

### Height Conversion

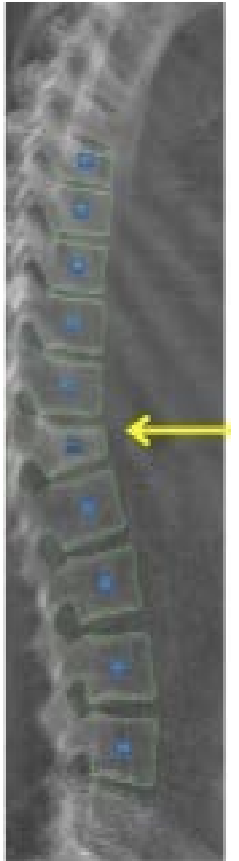
Inches   cm

**06053927**  
Individuals with fracture risk assessed since 1st June 2011

<https://www.sheffield.ac.uk/FRAX/tool.aspx>

# Vertebral Fracture Assessment (VFA)

- Densitometric spine imaging to detect vertebral fx.
- In **women  $\geq 70$  y, men  $\geq 80$  y** whose BMD T-score at the spine, total hip, or femoral neck is  $\leq -1.0$
- In **women 65-69 & men 70-79** whose BMD T-score at spine, total hip, or femoral neck  $\leq -1.5$
- **Postmenopausal women & men  $\geq 50$  with specific risk factors:**
  - Low trauma fracture
  - Historical height loss  $\geq 1.5$  inches (4 cm)
  - Prospective height loss of  $\geq 0.8$  inches (2 cm) since previously documented height measurement
  - Recent or ongoing long-term glucocorticoid treatment



# Laboratory Evaluation

- Biochemistry: Ca, PO<sub>4</sub>, albumin, Creatinine, liver enzymes including ALP, electrolytes
- 25-OHD
- CBC
- **Other labs:**
- SPEP, UPEP
- PTH, TSH
- 24 h urine calcium and creatinine
- Celiac screen, 24 h UFC
- Serum and urine markers of bone turnover: not routinely used in clinical practice, may be helpful in monitoring response to therapy

# Treatment

- **Supportive measures:**
  - **Calcium:** dietary preferably; if not then supplement total 1000-1200 mg/day
  - **Vit D:** 800-1000 IU daily; may need higher dose, target Vit D > 30 ng/ml
  - Regular **weight bearing** (e.g walking, jogging, Tai Chi, stair climbing, dancing, tennis) and **muscle strengthening exercise** (yoga, Pilates)
  - **Fall precautions**
  - **Smoking Cessation & avoiding excess alcohol intake**

## Estimating daily dietary calcium intake

Step 1: Estimate calcium intake from calcium-rich foods<sup>a</sup>

Product	# of servings/day	Estimated calcium/serving, in mg	Calcium in mg
Milk (8 oz.)	_____	×300	= _____
Yogurt (6 oz.)	_____	×300	= _____
Cheese (1 oz. or 1 cubic in.)	_____	×200	= _____
Fortified foods or juices	_____	×80 to 1,000 <sup>b</sup>	= _____
			Subtotal = _____
Step 2: Add 250 mg for nondairy sources to subtotal above			+250
			Total calcium, in mg = _____

# Pharmacologic Therapy

- **Choice of drug:** based upon efficacy, safety, cost, convenience and other patient related factors
  - Bisphosphonates
  - Denosumab
  - Teriparatide
  - Estrogen agonist/antagonist
- **Maintain normal s/Ca and Vit D level prior**

# Bisphosphonates

- 1<sup>st</sup> line drug of choice: effective, low cost, known long term safety data
- **Alendronate** or risedronate: both reduce vertebral and hip Fx
  - **Alendronate**: 70 mg PO weekly; Risedronate: 35 mg PO weekly
  - Ibadronate: 150 mg PO monthly; 3 mg IV q3mo (reduce vertebral fx)
  - **Zolendronate**: 5 mg IV yearly (reduce vertebral, hip and non vertebral fx)
- C/I:
  - Oral: Esophageal disorders, bariatric sx pts with surgical anastomosis (Roux-en-Y bypass)
  - CKD eGFR < 30 ml/min



# Denosumab: RANKL inhibitor

- Preferred for: high risk for fx, older pts who have difficulty taking oral or with markedly impaired renal function; intolerant or unresponsive to Bisphosphonates
- Reduce incidence of new vertebral, hip & nonvertebral fx in postmenopausal women → concern for increased risk of vertebral fx after discontinuation of therapy
  - Advised alternative therapy after discontinuation
- Dosing: 60 mg SQ q6month

# Anabolic agents: PTHrP analog

- Teriparatide & abaloparatide
- Stimulate bone formation & activate bone remodeling
- Preferred for: severe osteoporosis with high fx risk; OP with intolerance to bisphosphonates or with C/I to bisphosphonates; who fail other therapies i.e fx with loss of BMD in spite of compliance to therapy
- Dosing: 20 mcg SQ OD: **total max duration 2 yrs**
- Bone loss with rapid once stopped → initiate alternative Rx
- S/E: leg cramps, nausea, dizziness
- C/I: with increased risk of Osteosarcoma (Paget's dz, Prior Skeletal radiation), bone mets, Hypercalcemia, h/o Skeletal malignancy

# SERMS: Raloxifene

- Reduce risk of vertebral fx
- Indicated for reduction in risk of invasive breast cancer in postmenopausal women with OP
- Dose: 60 mg PO OD
- S/E: high risk of VTE, hot flashes, leg cramps

# THANK YOU



## References:

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