PHARMACIST CE:

Osteoporosis: A Pathophysiology and Pharmacotherapy Review Highlighting the Parathyroid Hormone Analogues and their Place in Therapy

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CE FOR **PHARMACISTS**

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Learning Objectives

- Explain the homeostatic functions of calcium, phosphorous, and parathyroid hormone (PTH) in the body.
- Differentiate the pathophysiology behind primary and secondary osteoporosis.
- List three risk factors for the development of osteoporosis.
- Identify two nonpharmacologic treatment options for osteoporosis management.
- Compare and contrast the treatment algorithms for osteoporosis according to the National Osteoporosis Foundation (NOF) and American Association of Clinical Endocrinology (AACE) guidelines.
- Describe the place in therapy of parathyroid hormone analogues for the treatment of osteoporosis.
- Design a treatment regimen for a patient who has severe or refractory osteoporosis.

While commonly perceived as a static organ system, the bones that make up the skeletal system are as dynamic as any other organ that comprises the human body. Bones are constantly growing, restructuring, and adapting to lifestyle and environmental changes.[1] Bones remain dynamic through two cell types, osteoclasts and osteoblasts. Osteoclasts cause the demineralization of bones and help "chew" up old bone so new bone can replace it.[1] Osteoblasts cause the mineralization of bones and help build new bone in place of old bone.[1] Osteoblasts and osteoclasts remain in a dynamic equilibrium with one another, constantly replacing old bone with new bone, releasing calcium and inorganic phosphate into the bloodstream when needed, and replacing those same minerals so bones do not become too brittle.[1] When the equilibrium between these two cells is disrupted, pathologic conditions such as osteoporosis occur.

Bones serve as a mineral reservoir for the body, storing 99% and 80% of the body's supply of calcium and inorganic phosphate, respectively.[2] Calcium and inorganic phosphate are stored in bones as a crystalline complex called hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$). Crystalline hydroxyapatite is the inorganic component of bone and accounts for about 60% of bone's composition. The remaining 40% is composed of about 10% water, and about 30% organic matter, such as proteins.[1] Bones have an array of functions, such as providing structural support and protecting vital organs. Bones also play a crucial role in maintaining mineral homeostasis.

Mineral homeostasis is maintained through the regulation of calcium resorption and deposition in the bones. Calcium is a crucial mineral in the body that carries out many physiologic and structural functions. It is regulated by parathyroid hormone (PTH), vitamin D, and calcitonin.[2] When serum calcium levels are low, PTH is released from the parathyroid gland. Parathyroid hormone inhibits osteoblast activity and activates

Abbreviations

AACE – American Association of Clinical Endocrinologists
BMD – Bone mineral density
BTM – Bone turnover markers
CCE – American College of Clinical Endocrinology
CKD – Chronic kidney disease
cAMP – Cyclic adenosine monophosphate
DM – Diabetes mellitus
DXA – Dual-energy X-ray absorptiometry
FDA – Food and Drug Administration
FRAX – Fracture Risk Assessment Tool
Fx(s) – Fracture(s)
IV – Intravenous
LS – Lumbar spine
MS – Multiple sclerosis
NOF – National Osteoporosis Foundation
NVFx(s) – Nonvertebral fracture(s)
PPI – Proton pump inhibitor
PTH – Parathyroid hormone
RA – Rheumatoid arthritis
RANKL – Receptor activator of the nuclear factor kappa-B ligand
RCT – Randomized controlled trial
RR – Risk ratio
SSRI – Selective serotonin reuptake inhibitor
SERM – Selective estrogen receptor modulator
SQ – Subcutaneous
VFx(s) – Vertebral fracture(s)
VFFx(s) – Vertebral fragility fracture(s)
WHO – World Health Organizatio

osteoclast activity, which results in increased bone resorption and release of calcium into the bloodstream.[2] Similarly, vitamin D aids in the intestinal absorption of calcium from the diet; increases in vitamin D result in decreased release of PTH, leading to an increase in serum calcium levels.[2] Calcitonin is secreted by the parafollicular cells of the thyroid gland and opposes the action of PTH.[2] When serum calcium levels are high, calcitonin is released from the thyroid gland to decrease intestinal absorption of calcium and prevent bone resorption.[2] This is achieved through inhibition of osteoclasts and activation of osteoblasts, which ultimately decreases serum calcium levels.

The interplay between PTH, vitamin D, calcium, and calcitonin, as well as the balance between osteoblast and osteoclast activity, is essential to healthy bone homeostasis. When these processes are disrupted, bone disease results and can lead to complications and decreased quality of life for patients. Osteoporosis is caused by increased osteoclast activity and decreased osteoblast activity, which leads to excessive bone demineralization.[1] The result of this osteoclast/osteoblast imbalance is brittle and porous bones, which can put patients at an increased risk for fractures.[1] Although nonpharmacologic considerations are an important aspect of osteoporosis management, pharmacologic treatment options, including bisphosphonates; the RANKL inhibitor denosumab; and the SERM raloxifene, are mainstays of treatment depending on patient history and risk.[8,10] This article will highlight the newer PTH analogues, teriparatide and abaloparatide, their mechanisms of action, as well as their place in the treatment of osteoporosis.

Pathophysiology, Epidemiology/Etiology, and Risk Factors

Osteoporosis is characterized by a decrease in bone density and mineralization, leading to porous and fragile bones that are at an increased risk of fracture. Osteoporosis is a multifactorial disease and can occur for varying reasons. Therefore, it is divided into different types: primary osteoporosis, further subdivided into type 1 and type 2; and secondary osteoporosis. Primary osteoporosis is the loss of bone density due to aging and decreased gonadal function; it is not due to any other chronic illness.[3] Type 1 primary osteoporosis occurs in postmenopausal women due to a drastic decline in estrogen production. Estrogen deficiency causes an activation of osteoclasts which leads to resorption pits in the bone. Osteoblasts cannot keep up with the high activity of osteoclasts, thus resulting in cortical and trabecular bone loss. Type 2 primary osteoporosis occurs in both men and women 70 years of age and older. It is caused by the progressive imbalance of bone resorption and formation as a result of hormone, calcium, and vitamin D deficiencies that occur with age. Like type 1, type 2 primary osteoporosis results in cortical and trabecular bone loss. Secondary osteoporosis is bone loss due to a chronic condition or medication; it is present in both men and women. Chronic conditions and medications that can lead to secondary osteoporosis are listed in Table 1.[4]

Bone strength relies heavily on bone quality and bone mineral density, which may be influenced by a variety of different factors including genetics, diet, lifestyle, hormonal status, medications and other medical conditions. Development of osteoporosis is more common with advanced age, and generally people older than 50 are most affected. Women are more likely to develop lower bone mass and osteoporosis than men. Therefore, two of the major risk factors include advanced age and gender (female). Other risk factors include race (White or Asian); body weight (less than 127 pounds) or small stature; estrogen deficiency before age 45; low physical activity; low calcium intake;

TABLE 1. Causes of Secondary Osteoporosis

Endocrine Disorders	Hyperparathyroidism or PTH excess, hyperthyroidism or thyroxine excess, hypogonadism, DM
Gastrointestinal Disorders	Inflammatory bowel disease, gastric bypass surgery, celiac disease
Hematologic Disorders	Multiple myeloma
Renal Disorders	CKD, idiopathic hypercalciuria
Autoimmune Disorders	RA, MS
Medications	Anticonvulsants, antidepressants (SSRIs), aromatase inhibitors, medroxyprogesterone, gonadotropin releasing hormone agonists, glucocorticoids, cytotoxic chemotherapy agents, thyroxine or thyroid hormone, immunosuppressants, antiretroviral agents, calcineurin inhibitors, PPIs, heparin, loop diuretics

cigarette smoking; 3 or more alcoholic beverages per day; an osteoporotic-related fracture; and rheumatoid arthritis.[5]

Patient Presentation and Diagnosis

Due to the silent nature of diminishing bone density, most patients will not present until they are post-fracture.[6] The most common areas for an osteoporotic fracture to occur are the hip, wrist, forearm, and vertebrae.[6] Patients may also present with symptoms such as pain, immobility, fear, or depression, although some fractures might also be asymptomatic.[6] Other signs of osteoporosis include shortened stature, kyphosis, lordosis, and an overall decrease in BMD.[6]

Assessment of BMD at multiple sites where osteoporotic fractures may occur is one of the most common methods for diagnosing osteoporosis.[6] DXA is considered the gold standard to predict bone mineral density and, thus, predict fracture risk.[6] Per the 2004 WHO Scientific Group on the Assessment of Osteoporosis at Primary Health Care Level, the standard for diagnosis based on BMD in men >/= 50 years old and postmenopausal women is a T-score 2.5 standard deviations or more below the normal range.[7] Per the AACE/ACE 2020 guidelines on postmenopausal osteoporosis, BMD testing is recommended in all women >/= 65 years old and younger postmenopausal women with an increased fracture risk.[8] Unless there are significant risk factors for diminished BMD, premenopausal women and otherwise healthy men are not recommended to undergo BMD measurement. BMD does remain the best indicator for fracture risk. However, BMD measurements should not be used alone. Combining BMD results with other fracture risk evaluations, such as the FRAX, might be recommended to help diagnose osteoporosis. FRAX is an algorithm applicable to men >40 years old and women at the age of menopause to calculate the 10-year probability of a hip or other osteoporotic fracture, with or without the bone mass density calculated at the femoral neck.[8] Risk factors included in FRAX are[8]:

- Ethnicity
- Age (must be between 40 and 90 years old)
- Sex
- BMI
- Family history of hip fractures
- Personal history of previous fractures considered fragile (radiographic vertebral fracture)
- Current or previous long-term glucocorticoid use
- Rheumatoid arthritis
- Current smoking

There are certain limitations to FRAX, which is why a combination of assessments to confirm diagnosis is best. FRAX does not account for how a vitamin D deficiency and recent or numerous falls might affect a patient's BMD. FRAX is also limited to patients who are treatment naïve, and assumes that a patient's fracture risk remains consistent over time.[9] Per the NOF 2014 guidelines on the prevention and treatment of osteoporosis, BMD testing should be performed via DXA in women >/= 65 years old, men >/= 70 years old, and postmenopausal women and men of younger ages who have other risk factors.[10] Based on the T-score, vertebral imaging may also be necessary. Vertebral imaging is necessary for women >/= 70 years old and men >/= 80 years old with a T-score </=-1, and postmenopausal women and men >/= 50 years old with certain risk factors, such as history of a trauma fracture, height loss, and long-term glucocorticoid treatment.[10] Annual height measurements should also be taken to observe whether there is any historical height loss of 1.5 inches or more.

Nonpharmacologic Treatment Options

There are a few non-pharmacologic treatments patients may incorporate into their lifestyles to help improve their bone health. These lifestyle modifications include limited alcohol intake, smoking cessation, weight-bearing and resistance exercise, fall prevention, and diet interventions.[6,9,11] There are several things to consider for dietary changes. As already stated, lower alcohol intake will benefit patients with osteoporosis. Excessive alcohol intake can lead to bone loss. Lowering caffeine and sodium intake will also yield some benefit. Caffeine may decrease calcium absorption, and high sodium intake will cause more calcium to be released, both of which can ultimately lead to lower bone density. Increased calcium and vitamin D may help with osteoporosis and can be found in foods like dairy products (milk, cheese, yogurt, etc.), leafy green vegetables (spinach, kale, etc.), soy beans, white beans, and certain types of fish. Patients may also consider including foods that are fortified to include more calcium, such as some orange juice and cereals. Foods that are rich in vitamin D include fatty fish (tuna, salmon, etc.), beef liver, cheese, and egg yolks. Just like calcium, there may also be certain foods fortified to include more vitamin D, such as dairy products, orange juice, and cereals.[9,11]

Calcium and Vitamin D Supplementation

Though increased dietary calcium and vitamin D intake is highly encouraged as the primary source, supplementation may be needed for most patients with osteoporosis to maintain calcium levels within normal limits. The daily recommended calcium and vitamin D supplement requirements are as follows[6,11]:

Calcium

Adolescents/Young Adults	1200-1500 mg
Men/Women Age 25-50	1000 mg
Men Age 51-70	1000 mg
Men Age >70	1200 mg
Women Age >50	1200 mg

Vitamin D

All Men	600 IU
Women Age 19-70	600 IU
Women Age >70	800 IU

Three different types of calcium are available for supplementation: calcium carbonate, calcium citrate, and tricalcium phosphate. When choosing among these types of supplements, providers and patients should consider cost, adverse effects, and patient preference. Calcium carbonate is typically the least expensive option for patients. However, this medication is best taken with food due to GI upset and requires adequate stomach acid to be well absorbed. Therefore, patients taking

stomach acid reducers such as proton pump inhibitors should refrain from using this source of calcium supplementation. For older patients, calcium citrate may be a better option, as it may be taken on an empty stomach and does not require stomach acid for absorption. Tricalcium phosphate is typically the agent used in most fortified foods and may be the most expensive supplementation option for patients. All products can cause adverse effects, including constipation, gas, and upset stomach. There is also an increased risk of kidney stone development from large calcium ingestion. Doses of calcium from all products should be limited to no more than 600 mg per dose.[6,9,11]

Treatment Guidelines

The AACE and ACE joint guidelines, along with the NOF guidelines, are the leading clinical references for guidance on the treatment of osteoporosis in men and postmenopausal women.[8,10] AACE/ACE guidelines include treatment recommendations for postmenopausal osteoporosis only, while the NOF guidelines also include recommendations for managing osteoporosis in men. The AACE/ACE and NOF guidelines differ slightly in their recommendations for when pharmacologic treatment for osteoporosis should be initiated. AACE/ACE guidelines recommend treatment initiation in patients with a T-score ≤-2.5 in the lumbar spine, femoral neck, total proximal femur, or ⅓ radius, in patients with low-trauma spine or hip fractures; and in patients with a T-score between -1 and -2.5 along with the presence of fragility fractures or high FRAX.[8] NOF guidelines recommend pharmacologic treatment initiation in patients with hip or vertebral fractures; in patients with a T-score ≤-2.5 at the femoral neck, total hip, or lumbar spine; and in men and women age 50 or older who have a T-score between -1 and -2.5 along with an elevated 10-year hip fracture probability based on FRAX.[10]

Prior to initiation of pharmacologic therapy, patients should be assessed for any secondary causes of osteoporosis, including endocrine, gastrointestinal, and medication-related causes, examples of which are listed in Table 1. Both the AACE/ACE and the NOF guidelines also recommend initiating the aforementioned nonpharmacologic treatment options, including smoking cessation, alcohol use reduction, and fracture risk assessment strategies for patients diagnosed with osteoporosis.[8,10] In addition, any calcium or vitamin D deficiencies should be corrected through diet or supplementation in order to maintain appropriate calcium intake as well as a serum 25-hydroxyvitamin D (25[OH] D) level ≥ 30ng/mL.[8,10]

The AACE/ACE guidelines include an algorithm to guide the treatment of osteoporosis in postmenopausal women, which stratifies treatment modalities based on history of fractures and risk for future fractures.[8] In patients with no history of prior fractures who are deemed to be at high risk, the bisphosphonates alendronate, risedronate, and zoledronate are considered first-line therapeutic options, along with the bone-modifying monoclonal antibody denosumab.[8] Bisphosphonates indirectly increase BMD by acting on osteoclasts and osteoclast precursors, which ultimately leads to inhibition of bone resorption.[12] Denosumab binds RANKL to prevent osteoclast formation and also leads to a decrease in bone resorption.[13] Alternative agents include the bisphosphonate ibandronate, and raloxifene, a SERM, which antagonizes bone tissue to prevent bone loss.[14] Patients should be assessed yearly for fractures and progression or improvement in BMD.[8] If there is improvement in BMD without the occurrence of fractures, clinicians should consider a drug holiday after five years of oral therapy and three years of IV therapy.[8] Therapy should be re-initiated in patients who develop fractures, have a significant decline in BMD, or have BTM that rise to pretreatment levels.[8]

Based on the AACE/ACE guidelines, high-risk patients without fracture history who have further bone loss or fracture occurrence on first-line therapies should be assessed for causes of inadequate therapeutic response.[8] Adherence, as well as the development of any secondary causes of osteoporosis, should be reviewed prior to

TABLE 2. Dosing and Administration Pearls for the Parathyroid Hormone Analogues[16,17]

Drug	*FDA Indication(s) and Dose(s)*	*Administration*
Teriparatide (Forteo)	Postmenopausal osteoporosis in women with a high fracture risk: • **Treatment:** 20mcg SQ daily Increase bone mass in males with primary or hypogonadal osteoporosis with a high fracture risk: • **Treatment:** 20mcg SQ daily Glucocorticoid-induced osteoporosis in men and women with a high fracture risk receiving ≥5mg/day of prednisone equivalent: • **Treatment:** 20mcg SQ daily	• For first administration, ensure patient is in an environment where they can sit/lie down in the event of orthostasis • Inject into thigh or abdominal wall • Can be administered without regard to time or meals • Can administer right after removal from refrigeration • Each device good for 28 days after first use • Can be used for up to 2 years
Abaloparatide (Tymlos)	Postmenopausal osteoporosis in women with a high fracture risk: • **Treatment:** 80mcg SQ daily	• For first administration, ensure patient is in an environment where they can sit/lie down in the event of orthostasis • Inject into the periumbilical region of the abdomen • Rotate injection site daily • Administer at the same time every day • Can be used for up to 2 years

therapeutic escalation. In the absence of any identifiable causes of disease progression, patients previously on oral agents should be switched to injectable antiresorptive agents, or transitioned to the parathyroid hormone analogues abaloparatide or teriparatide, or the sclerostin inhibitor romosozumab.[8] The pharmacology and mechanism of action of the parathyroid hormone analogues will be discussed shortly. Romosozumab is a monoclonal antibody that increases bone formation through activation of the Wnt/Beta-catenin signaling pathway.[15]

The AACE/ACE postmenopausal osteoporosis treatment algorithm also stratifies treatment for patients who have a history of prior fractures and are at a very high fracture risk, which includes patients who are frail, elderly, have an increased fall risk, who use glucocorticoids, or who have very low T-scores.[8] First-line agents for such patients include abaloparatide, denosumab, romosozumab, teriparatide, and zoledronate. Alternative agents include alendronate and risedronate.[8] These patients should also have yearly assessments to monitor adherence, disease progression, and fracture occurrence.[8] Patients should receive denosumab until they are no longer deemed to be very high risk, and should then be transitioned to an appropriate antiresorptive agent.[8] Romosozumab should be trialed for one year, and then patients should be transitioned to an appropriate IV or oral antiresorptive agent as well.[8] The parathyroid hormone analogues can be used for up to two years before transitioning to an antiresorptive agent, and zoledronate can be continued for up to six years before a drug holiday is recommended.[8] If patients do not respond, or experience fractures while taking zoledronate, they can be switched to a parathyroid hormone analogue or romosozumab in order to prevent further disease progression.[8]

PTH Analogue Pharmacology, Dosing, and Administration

The parathyroid hormone analogues teriparatide and abaloparatide are both FDA-approved for the treatment of postmenopausal osteoporosis in women with a high risk for fractures. Teriparatide is also FDA-approved to increase bone mass in men with hypogonadal osteoporosis, along with glucocorticoid-induced osteoporosis in both men and women. These agents contain a recombinant amino acid sequence that is identical to the N-terminal of parathyroid hormone, and thus increase BMD and bone mass through stimulation of osteoblast function.[16,17] Teriparatide and abaloparatide achieve their pharmacologic activity by increasing the concentration of cAMP upon binding to the PTH Type 1 receptor.[18] Although analogues of PTH, teriparatide and abaloparatide have a lesser effect on calcium compared to endogenous PTH.[18] Adverse effects of these agents include, headache, dizziness, nausea, and an increased risk for osteosarcoma.[16,17] In addition, their duration of therapy should not exceed 24 months.[16,17]

The Fracture Prevention Trial was the first randomized controlled trial that assessed the efficacy of teriparatide for the treatment of osteoporosis in postmenopausal women.[19] Neer and colleagues found that teriparatide could significantly reduce the incidence of VFxs and NVFxs by 65% and 53%, respectively, compared to placebo.[19] They also compared different doses of teriparatide, and found that both the 20mcg dose and the 40mcg dose significantly increased BMD at the LS, femoral neck, trochanter, intertrochanter, and total hip ($p<0.001$).[19] Originally planned for a duration of 24 months, the study was discontinued early due to the incidence of osteosarcoma in long-term rat toxicology studies.[19] The average treatment duration was 18 months; however, no human cases of osteosarcoma were reported.[19]

The VERO trial compared teriparatide 20ug daily versus risedronate 35mg weekly for the prevention of new VFx in postmenopausal women with osteoporosis.[20] Treatment lasted for up to 24 months, and subgroup analyses were performed to stratify outcomes based on the number of prevalent VFFxs, the severity of Fxs, the number of prevalent NVFxs, the use of glucocorticoids, and a history of prior pharmacologic treatment for osteoporosis.[20] For the entire study population, VFxs occurred in 5.4% of women in the teriparatide group and 12.0% in the risedronate group, with a RR 0.44 (95% CI: 0.29-0.68; $p=0.000094$).[20] Overall, about half as many patients who received teriparatide experienced a VFx compared to patients who had received risedronate.

The ACTIVE trial was a Phase III, double-blind, international RCT that compared the incidence of new VFx and NVFxs in osteoporotic postmenopausal women treated with either abaloparatide or placebo.[21] Postmenopausal women ≥65 years of age fulfilling the fracture and T-score criteria (≤2.5 SD and >5 SD) or those with severe osteoporosis without fracture (≤3.0 SD but >5 SD) were enrolled.[21] Abaloparatide treatment reduced the absolute risk of new morphometric VFx by 3.6% (0.6% vs. 4.2%) compared to placebo, corresponding to a relative risk reduction of 86% ($P < 0.001$).[21] Abaloparatide treatment after 18 months increased BMD for the total hip, femoral neck, and LS by 4.25%, 4.01%, and 10.4%, respectively, compared to placebo.[21]

The ACTIVExtend trial further expanded on the findings of the ACTIVE trial, and showed that patients who received alendronate after abaloparatide had a reduced risk of fracture at total hip, femoral neck, and LS compared to patients that had received placebo prior to alendronate therapy.[22] In addition, BMD at the spine and total hip continued to increase during the 24-month alendronate treatment period following the initial 18 months of abaloparatide therapy.[22] Discontinuation of abaloparatide led to more serious events in 9.9% of patients compared to placebo (6.1%) or teriparatide (6.8%).[22] Table 2 includes the specific dosing and administration recommendations for the FDA-approved indications for teriparatide and abaloparatide.

Conclusion

Osteoporosis is a spectrum of bone disease characterized by compromised bone integrity and an increased risk for fractures.[10] The development of osteoporosis is multifactorial, and often involves an interplay between environmental, genetic, and hormonal factors.[8,10] BMD measured through DXA is considered the gold standard for the diagnosis of osteoporosis, although FRAX can also be a useful tool to stratify fracture risk.[7] The NOF and the AACE/ACE guidelines provide recommendations on both nonpharmacologic and pharmacologic treatment approaches to osteoporosis, with an emphasis on ruling out secondary causes of osteoporosis and addressing underlying

calcium and vitamin D deficiencies prior to pharmacologic treatment initiation.[8,10]

Available as SQ formulations, teriparatide and abaloparatide are reserved for treatment-resistant and more severe cases of osteoporosis.[8] In patients without prior fracture history who are at a high risk for developing fractures, teriparatide and abaloparatide are second-line options for those who have worsening disease on first-line therapeutic options, such as bisphosphonates or denosumab.[8] In high-risk patients with a history of fractures, teriparatide and abaloparatide are considered first-line treatment options. Treatment duration of these agents is, however, limited to 2 years, at which point patients should be transitioned to an appropriate antiresorptive therapy.[8,16,17]

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Patient Case

The patient (known as "PB") is a 71-year-old, postmenopausal (at age 53), White female. She has a history of high blood pressure, COPD, and GERD. No history of fracture. Her current medications include amlodipine 5 mg po daily, Combivent Respimat® 1 puff QID, hydrochlorothiazide 25 mg po daily, and pantoprazole 40 mg po daily. She does not take any over-the-counter medications. She denies any medication allergies or adverse drug reactions. Her calcium intake from her diet is estimated to be 200 mg daily.

She does not regularly exercise. She walks once weekly for 20 minutes.
Caffeine: 3 cups per day
Alcohol: 1 drink (wine or beer) 3 days per week
Tobacco: Former smoker, smoked 1 ppd for 15 years, quit 40 years ago.
Illicit drugs: Denies
PB weighs 120 pounds and is 63 inches tall.

Labs		**Reference Range**
WBC	6.7	3.7-10.5 k/mm3
Hemoglobin	14.2	11.9-15.5 g/dL
Hematocrit	41%	35-47%
Platelets	289	50-400 k/mm3
Red Blood Count	4.4	4.0-5.2 millions/mm3
RDWCV	11.3	9.0-14.5%
RDWSD	40.2	36.4-46.3 fL
MCV	88	82-99 femtoliters
MPV	10.9	9.4-12.3 fL
MCH	29	25-35 picograms
MCHC	33	32-36 g/dL RBC
Albumin	4.2	3.4-5.4 g/dL
Alk Phos	63	20-130 U/L
ALT	19	4-36 U/L
AST	22	8-33 U/L
BUN	16	6-20 mg/dL
Calcium	8.2	8.5-10.2 mg/dL
Chloride	100	96-106 mEq/L
CO2	25	23-29 mEq/L
Creatinine	1.2	0.6-1.3 mg/dL
Glucose	94	70-100 mg/dL
Potassium	4.3	3.7-5.2 mEq/L
Sodium	140	135-145 mEq/L
Total bilirubin	0.8	0.1-1.2 mg/dL
Total Protein	7.1	6-8.3 g/dL
TSH	4.2	0.5-6 uU/mL
Free T4	1.1	0.7-1.9 ng/dL
Free T3	400	230-619 pg/d
Total Cholesterol	190	125-199 mg/dL
LDL	80	<100 mg/dL
Triglycerides	140	<150 mg/dL
HDL	58	>50 mg/dL
Vitamin D	33 ng/mL	>20 ng/mL
T score (DXA spine)	-2.9	
T score (DXA femoral neck)	-2.7	
Creatinine Clearance	37 mL/min	

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Assessment Questions

1. Which of PB's lab values is the most important to assess when evaluating PB for osteoporosis?
   a. Calcium
   b. Creatinine
   c. TSH
   d. Vitamin D

2. Which of the following medications could be contributing to PB's osteoporosis?
   a. Amlodipine
   b. Combivent®
   c. Hydrochlorothiazide
   d. Pantoprazole

3. How many risk factors for osteoporosis does PB have?
   a. 2
   b. 3
   c. 6
   d. 11

4. What is an appropriate calcium and vitamin D regimen to recommend for PB?
   a. Calcium carbonate 1200mg PO once daily and vitamin D 800 units once daily
   b. Calcium citrate 1200mg PO once daily and no vitamin D
   c. Calcium citrate 500mg PO BID and vitamin D 800 units once daily
   d. No supplementation is necessary

5. **True or False:** According to the AACE/ACE 2020 Postmenopausal Osteoporosis Treatment Algorithm, PB is considered at very high risk.
   a. True
   b. False

6. Which of the following is an appropriate first-line therapy for PB?
   a. Alendronate 70mg PO once weekly
   b. Calcitonin 200units IN daily
   c. Romosozumab 210mg SQ once monthly
   d. Teriparatide 20mg SQ once daily

7. Three years later, PB is admitted with a vertebral fracture, and her T-score is -3.4. PB's physician decides to start teriparatide 20mg SQ once daily. What is the expected length of teriparatide therapy?
   a. 6 months
   b. 1 year
   c. 2 years
   d. 5 years

8. Which of the following adverse effects is associated with teriparatide?
   a. Cardiac disorders
   b. Hypocalcemia
   c. Orthostatic hypotension
   d. Osteonecrosis of the jaw

9. Did the activity meet the stated learning objectives? (if you answer no, please email sarahs@pswi.org to explain)
   a. Yes
   b. No

10. On a scale of 1 – 10 (1-no impact; 10-strong impact), please rate how this program will impact the medication therapy management outcomes or safety of your patients.

11. On a scale of 1 – 10 (1-did not enhance; 10-greatly enhanced), please rate how this program enhanced your competence in the clinical areas covered.

12. On a scale of 1 – 10 (1-did not help; 10-great help), please rate how this program helped to build your management and leadership skills.

13. How useful was the educational material?
   a. Very useful
   b. Somewhat useful
   c. Not useful

14. How effective were the learning methods used for this activity?
   a. Very effective
   b. Somewhat effective
   c. Not effective

15. Learning assessment questions were appropriate.
   a. Yes
   b. No

16. Were the authors free from bias?
   a. Yes
   b. No

17. If you answered "no" to question 16, please comment (email info@pswi.org).

18. Please indicate the amount of time it took you to read the article and complete the assessment questions.

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Quiz Answer Form

circle one answer per question

1) a b c d
2) a b c d
3) a b c d
4) a b c d
5) a b
6) a b c d
7) a b c d
8) a b c d
9) a b
10)_____
11)_____
12)_____
13) a b c
14) a b c
15) a b
16) a b
17)_____
18)_____

November/December 2021
Osteoporosis: A Pathophysiology and Pharmacotherapy Review Highlighting the Parathyroid Hormone Analogues and their Place in Therapy

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