Kaplan USMLE Step 1 prep: What drug worsens severe low back pain?

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If you're preparing for the United States Medical Licensing Examination® (USMLE®) Step 1 exam, you might want to know which questions are most often missed by test-prep takers. Check out this example from Kaplan Medical, and read an expert explanation of the answer. Also check out all posts in this series.

This month's stumper

A 66-year-old woman comes to the physician because of severe lower back pain. She is otherwise healthy with well-controlled hypertension and hyperlipidemia. She does not drink, but has smoked one pack of cigarettes per day for the past 20 years. An x-ray of the lumbar spine shows an anterior wedge compression fracture of L1. Results of dual-energy X-ray absorptiometry (DEXA) scan shows substantially decreased bone density in the region of L3 to S1. Laboratory studies show serum calcium of 9.2 mg/dL, serum phosphorus of 3.7 mg/dL, and serum parathyroid hormone of 42 pg/mL (normal range: 10-60 pg/mL).

Which of the following drugs is most likely to exacerbate this patient's condition?

A. Calcitonin.

B. Conjugated estrogens.

C. Cortisone.

D. Hydrochlorothiazide.

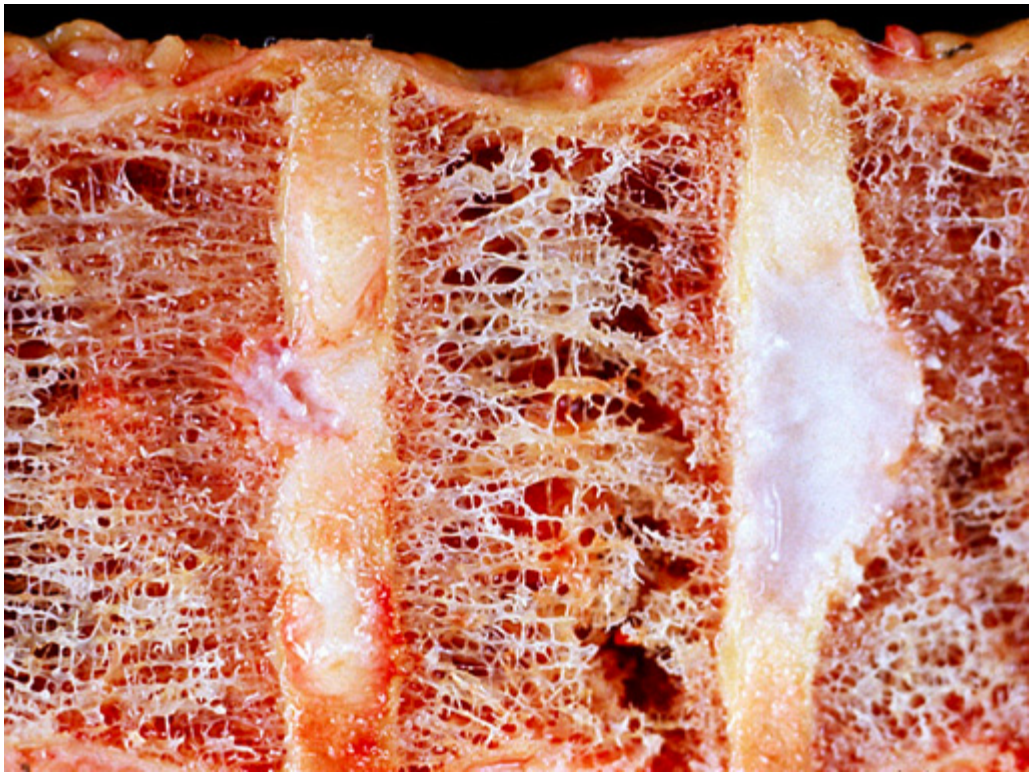
E. Risedronate.

F. Vitamin D.

The correct answer is C.

Kaplan Medical explains why

Our patient presents with a vertebral fracture and decreased bone density, pointing towards osteoporosis as the underlying disease process (see figure). She has classic risk factors including post-menopausal age and a history of smoking. Glucocorticoids should be avoided in these patients, because they accelerate bone resorption while inhibiting formation; thus, their use is associated with early rapid bone loss. With chronic use, suppression of bone formation becomes the predominant skeletal effect. The decrease in bone formation is mediated by direct inhibition of osteoblast proliferation and differentiation. Glucocorticoids also decrease intestinal calcium absorption, in part by opposing the effects of vitamin D as well as decreasing the expression of calcium channels in the duodenum. The glucocorticoids also increase renal calcium excretion by decreasing calcium reabsorption.



A diagnosis of osteoporosis is based on prior history of a "fragility" fracture or low bone mass density, which is defined as a bone densitometry T-score less than 2.5. Although calcium can be part of an osteoporosis treatment regimen, patients typically have normal serum levels of calcium. Normal levels of phosphorus, alkaline phosphatase, and parathyroid hormone (PTH)* are often present as well.

Histologic bone sections generally show thin trabeculae that have normal calcification and normal amounts of osteoblasts and osteoclasts. There are two general classes of osteoporosis: primary and secondary. Primary osteoporosis is the most common type and generally occurs in postmenopausal women secondary to low estrogen levels. Secondary osteoporosis results from other medical therapies and/or conditions, including glucocorticoid use, hyperthyroidism, and hypogonadism.

*(Note that the PTH reference range provided under the laboratory values table tab [230–630 pg/mL] is based on published NBME laboratory values. These data may be based on early PTH assays which were erroneously responding to other proteins in addition to PTH. More modern assays give PTH reference intervals in the 10–55 pg/mL range, although some studies suggest the low end of the range may be closer to 1 pg/mL).

Why the other answers are wrong

Choice A: Calcitonin inhibits osteoclast activity, increases osteoblast activity, and helps regulate plasma calcium levels via bone, renal, and gastrointestinal effects. It can help slow bone loss and stabilize elevated calcium levels, thus having therapeutic use in Paget disease, hypercalcemia, and postmenopausal osteoporosis.

Choice B: Conjugated estrogens are generally considered only for postmenopausal women at high risk for osteoporosis in whom non-estrogen medications are inappropriate. Estrogens reduce osteoclast activity by inhibiting IL-1. Risks of hormone therapy include increased risk of heart disease, stroke, and breast cancer.

Choice D: Hydrochlorothiazide is a thiazide diuretic used for the treatment of various edematous states and hypertension. Although most diuretics (e.g., furosemide and torsemide) decrease calcium levels, hydrochlorothiazide increases blood calcium levels. The thiazides inhibit the Na+-Cl– symport in the distal convoluted tubule, which reduces intracellular Na+ concentration and thereby enhances the voltage gradient driving passive Ca2+ influx across the apical membrane. This results in increased Ca2+ reabsorption and potentially hypercalcemia, which should not worsen this patient's condition.

Choice E: Risedronate is a bisphosphonate used for both treatment and prevention of postmenopausal osteoporosis. It acts by inhibiting osteoclast activity, reducing bone resorption and turnover.

Choice F: Vitamin D stimulates intestinal calcium and phosphorus absorption and stimulates bone mineralization. It is used in the treatment of postmenopausal osteoporosis.

Tips to remember

- Glucocorticoids can cause various musculoskeletal alterations, including bone matrix atrophy (osteoporosis) and bone fractures (vertebral compression fractures or fractures of long bones and avascular necrosis of femoral or humeral heads, or both).
- Postmenopausal women should be monitored for signs of osteoporosis during any extended course of corticosteroid therapy.

For more prep questions on USMLE Steps 1, 2 and 3, view other posts in this series.