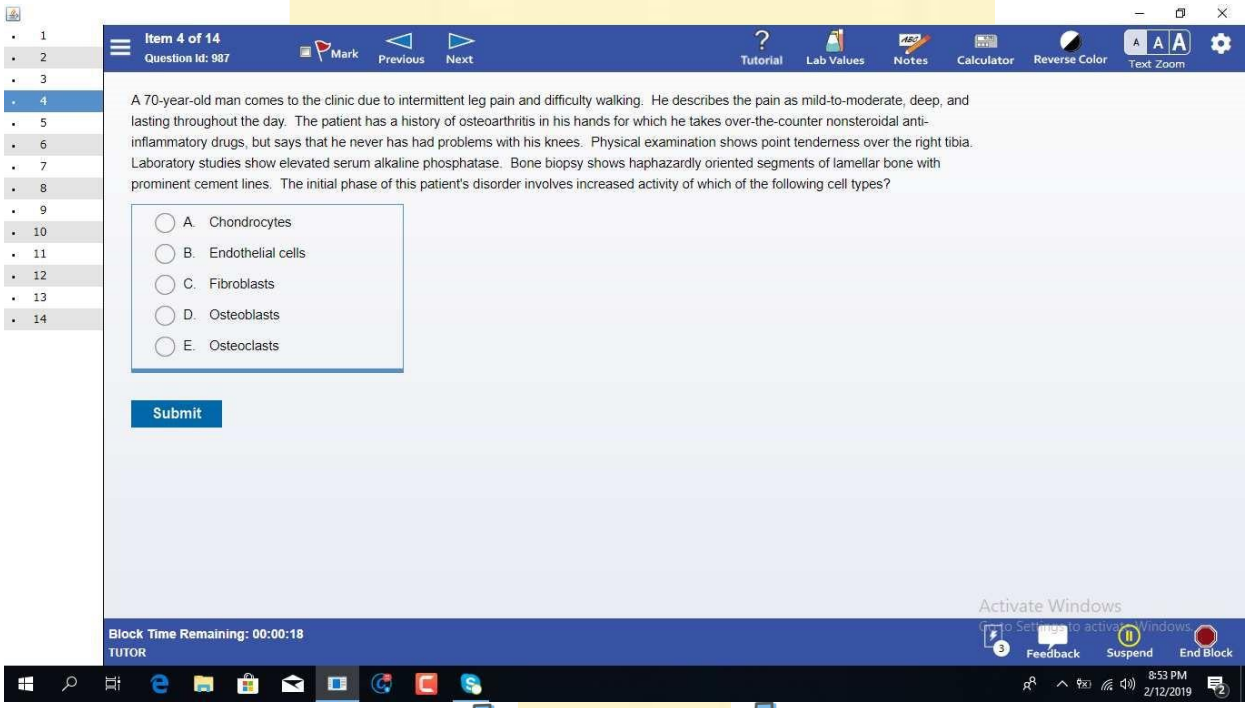
MSS

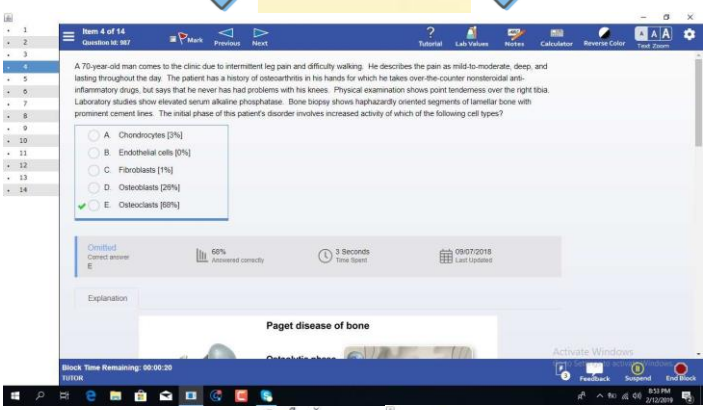
15 USMLE QUESTIONS
(UWORLD + RX)
With clarifications

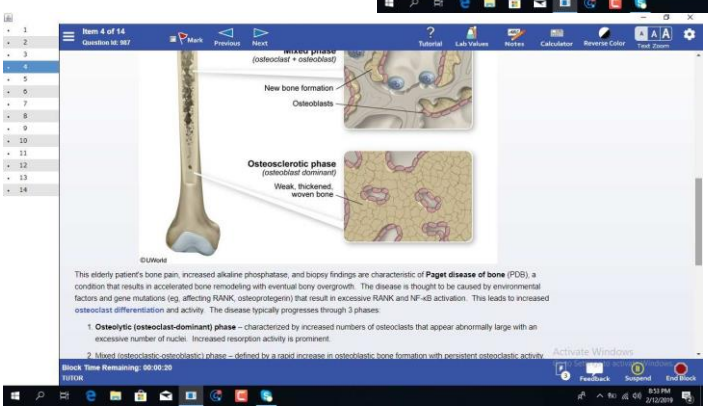
First 3 lectures of pathology

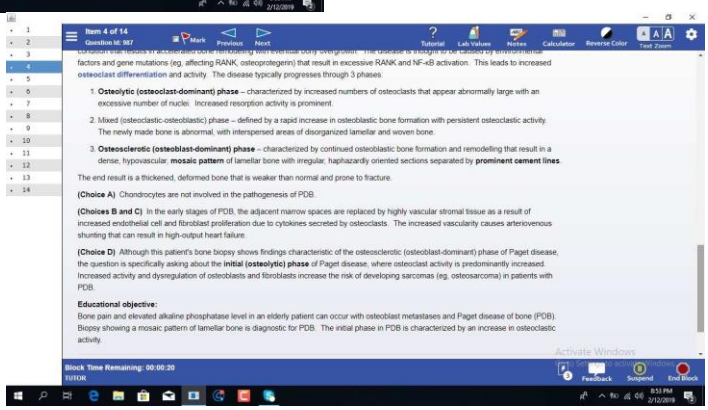
USMLE-UWORLD Test Bank

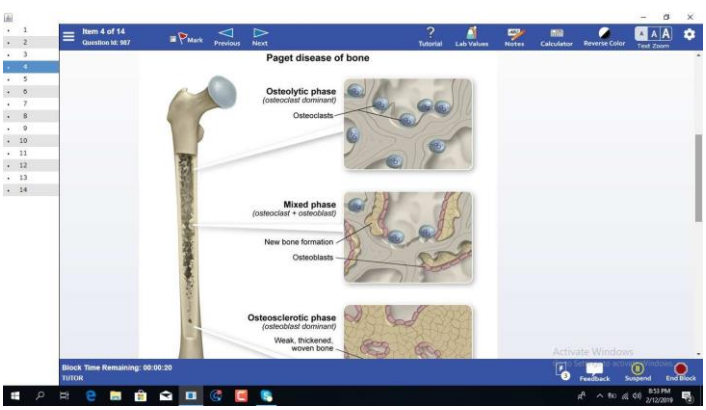


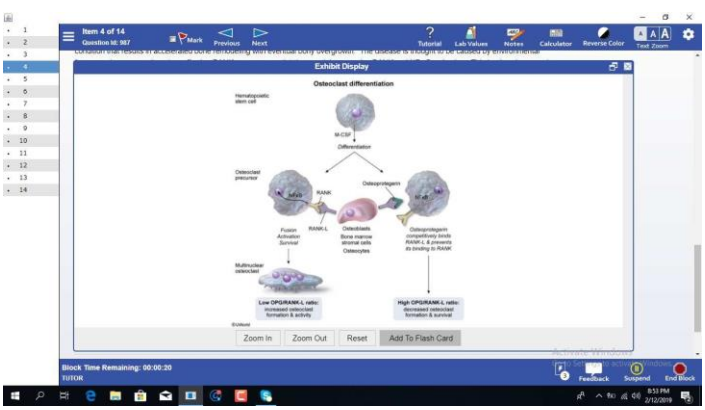
Answer

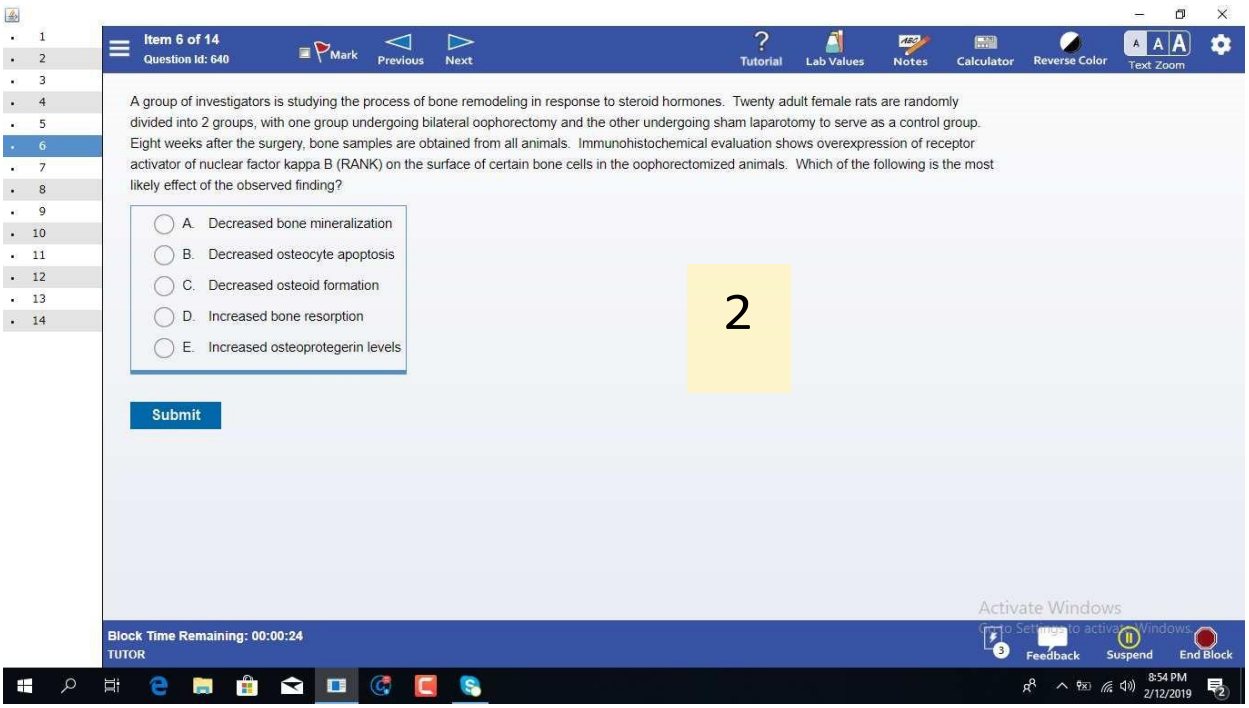











Item 6 of 14
Question Id: 640
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A group of investigators is studying the process of bone remodeling in response to steroid hormones. Twenty adult female rats are randomly divided into 2 groups, with one group undergoing bilateral oophorectomy and the other undergoing sham laparotomy to serve as a control group. Eight weeks after the surgery, bone samples are obtained from all animals. Immunohistochemical evaluation shows overexpression of receptor activator of nuclear factor kappa B (RANK) on the surface of certain bone cells in the oophorectomized animals. Which of the following is the most likely effect of the observed finding?
A. Decreased bone mineralization
B. Decreased osteocyte apoptosis
C. Decreased osteoid formation
D. Increased bone resorption
E. Increased osteoprotegerin levels
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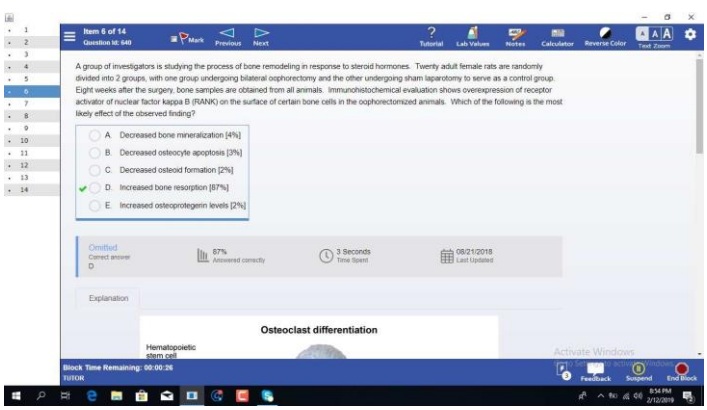
Answer


Item 6 of 14
Question Id: 640
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A. Decreased bone mineralization [4%]
B. Decreased osteocyte apoptosis [3%]
C. Decreased osteoid formation [2%]
D. Increased bone resorption [87%]
E. Increased osteoprotegerin levels [2%]
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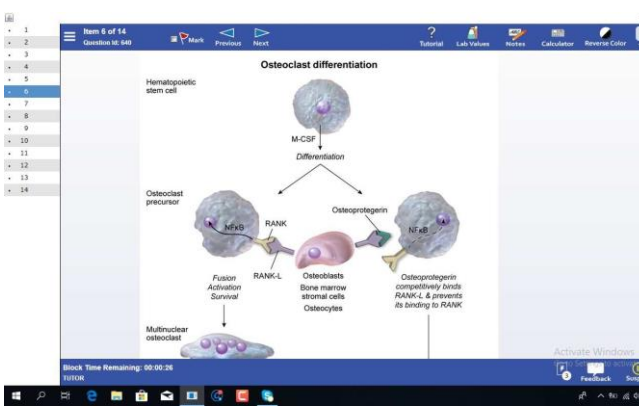
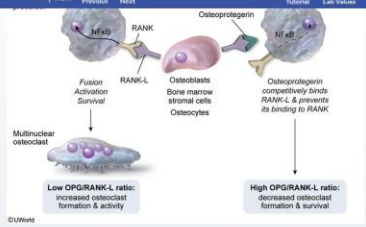
Explanation
Osteoclast differentiation
Hematopoietic stem cell


Osteoclast differentiation
Hematopoietic stem cell
M-CSF
Differentiation
Osteoclast precursor
RANK
Osteoprotegerin
NFκB
RANK-L
Fusion
Activation
Survival
Osteoblasts
Bone marrow stromal cells
Osteocytes
Osteoprotegerin competitively binds RANK-L & prevents its binding to RANK
Multinuclear osteoclast



The 2 most important factors in osteoclast differentiation are macrophage colony-stimulating factor (**M-CSF**) and receptor activator of nuclear factor kappa B ligand (**RANK-L**), which stimulate the development of mature, multinucleated osteoclasts. The interaction of RANK-L with RANK (receptor) is blocked by **osteoprotegerin** (OPG), which acts as a decoy receptor. By binding RANK-L, OPG reduces the differentiation and survival of osteoclasts, resulting in decreased bone resorption and increased bone density. Bone turnover is therefore regulated by the **ratio of OPG to RANK-L**; bone turnover increases when OPG is low and RANK-L is high.

Estrogen maintains bone mass in premenopausal women by inducing the production of OPG by osteoblasts and stromal cells. It also decreases the expression of RANK on osteoclast precursors. By contrast, the **loss of estrogen effect** (eg, menopause, oophorectomy) increases the

Item 11 of 14
Question Id: 700

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A 24-year-old woman comes to the office at 12 weeks gestation for prenatal counseling. She is 120 cm (3 ft 11 in) tall with short upper and lower extremities but normal torso length. Physical examination is also significant for depression of the nasal bridge and a bulging forehead. Her husband is phenotypically normal and has no medical problems. The patient knows that there is a 50% chance of passing on her condition to the fetus. An abnormality involving which of the following cells is most likely responsible for this patient's features?

- A. Chondrocytes
- B. Hypothalamic neurosecretory cells
- C. Osteoblasts
- D. Osteoclasts
- E. Pituitary somatotrophs

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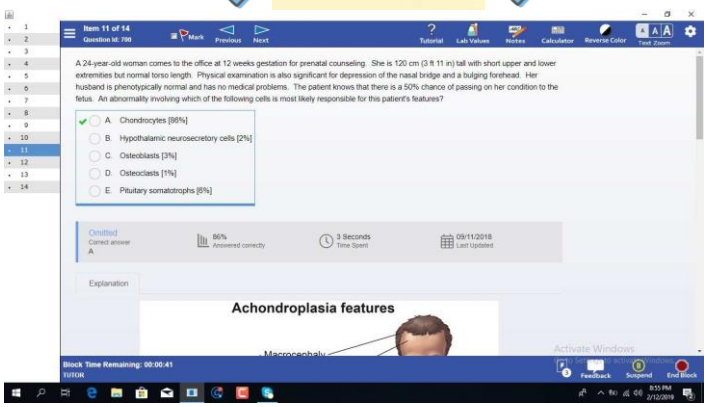

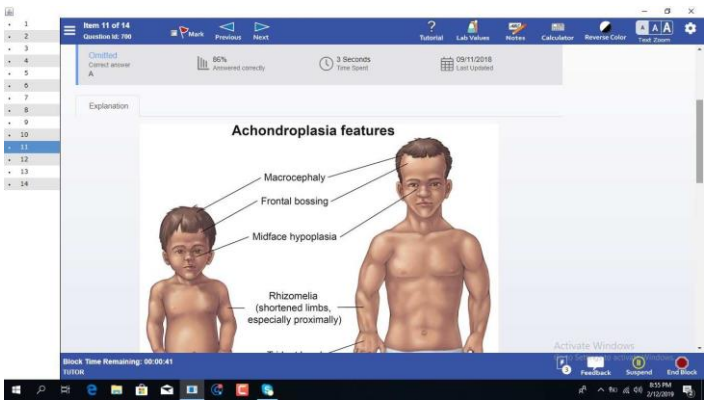

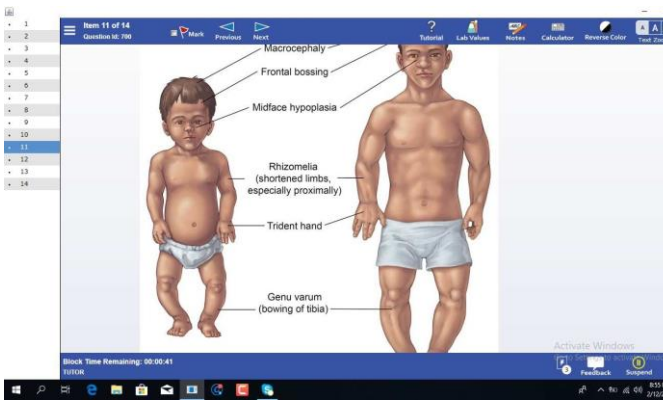

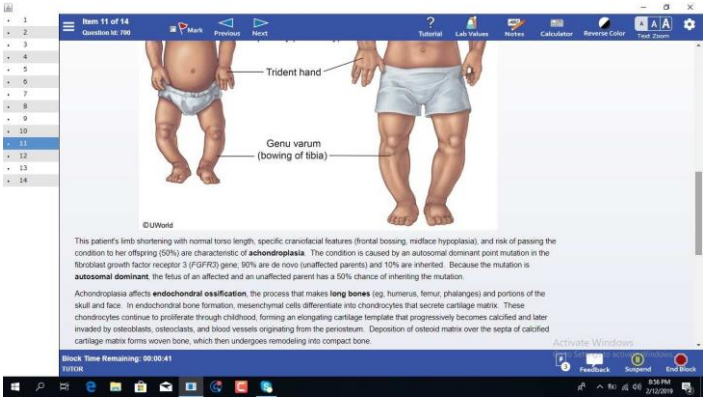

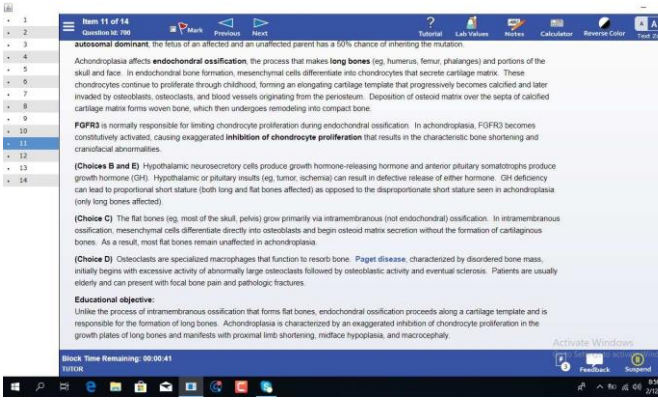

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A 35-year-old man is brought to the emergency department because of multiple rib fractures after a low-speed motor vehicle collision. No one else involved in the crash was injured. Laboratory findings are as follows.

Calcium: 15.3 mg/dL
Phosphate: 1.8 mg/dL
Alkaline phosphatase: 172 IU/L.

A radiograph of the patient's femur is shown.

Image courtesy of Khooula BA et al. Case Rep Orthop 2011;2011:521578

1

End Block

Based on the laboratory and image findings, which of the following is the most likely diagnosis?

- **A.** Osteitis fibrosa cystica
- **B.** Osteomalacia
- **C.** Osteopetrosis
- **D.** Osteosarcoma
- **E.** Paget's disease

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Item: 2 of 13
QID: 1800.13

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A 59-year-old woman who has a 5-year history of type 2 diabetes mellitus comes to her primary care physician for a routine visit. Her last Hb A1c 1 year ago was 9% and she was told to improve her diet and to exercise regularly. She was also started on metformin 1500 mg daily; however, she has not taken her medication consistently. Today, she notes that she was recently in the emergency department for a humeral fracture; she states that she is still confused because she "didn't fall that far." On evaluation today, her temperature is 37.7° C (99° F), blood pressure is 130/90 mm Hg, pulse is 75/min, and respiratory rate is 18/min. Routine laboratory results show a creatinine of 2.1 mg/dL. Her last creatinine 1 year ago was 1 mg/dL.

Given the patient's laboratory findings, she is most likely developing which of the following conditions?

- **A.** Hypokalemia
- **B.** Hypophosphatemia
- **C.** Hypotension
- **D.** Metabolic alkalosis
- **E.** Polycythemia
- **F.** Renal osteodystrophy

2

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A 62-year-old white woman comes to her family doctor because of of lower back pain located over the spine. When asked about the onset o pain, she does not recall any recent trauma. She has had no significant weakness, sensory changes, numbness, or tingling. She additionally denies any recent fevers, night sweats, or weight loss. Her past medical history is significant for severe osteoarthritis of the knees for the pa 10 years, which has significantly limited her physical activity. She otherwise has no chronic medical problems and takes only ibuprofen to help with her knee pain. A radiograph of the spine was obtained.

Option	Calcium	Phosphorus	Alkaline phosphatase
A	Decreased	Increased	Normal
B	Normal	Normal	Normal
C	Normal	Normal	Increased
D	Increased	Decreased	Increased
E	Decreased	Decreased	Increased

Image courtesy of William Scott, MD

3

Which of the following sets of serum laboratory findings is most likely in this patient?

- **A.** A
- **B.** B
- **C.** C
- **D.** D
- **E.** E

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Mark | Previous | Next | Lab Values | Notes | Calculator | Reverse Color | Text Zoom

A 3-year-old boy is brought to his pediatrician's office for a well-child exam. His family emigrated from Kenya last year and he is fully vaccinated. Up until the age of 8 months, he was exclusively breastfed. Since that time, he has consumed a diet consisting primarily of vegetables, fruits, and eggs. He is otherwise healthy with no past medical conditions. On physical examination, the physician notes the patient's dark skin as well as widening of the wrist bones and wide-spacing of the cranial sutures that is easily reducible by pressure. An x-ray of the child's lower extremities is shown.

4

Which of the following is most likely responsible for this patient's condition?

- **A.** Decreased alkaline phosphatase (ALP)
- **B.** Deficiency of parathyroid hormone
- **C.** Impaired bone mineralization
- **D.** Malabsorption of fat-soluble vitamins
- **E.** Mutation of type I collagen
- **F.** Renal phosphate wasting

Suspend

A 67-year-old woman with a history of breast cancer visits her physician with some shortness of breath and back pain. She takes no medications. X-ray of the chest shows no evidence of infection but discloses a thoracic vertebral fracture. Given the patient's age and gender, the physician obtains a dual energy x-ray absorptiometry (DEXA) scan, which reveals 30% bone loss throughout her spine, humerus, and femur. She prescribes a medication. One month later, the patient presents to the emergency department with dysphagia and burning chest pain and is admitted for treatment.

Which of the following drugs was most likely prescribed by the physician and subsequently caused the patient's dysphagia and burning chest pain?

- A. 25-Hydroxyvitamin D
- B. Alendronate
- C. Denosumab
- D. Estradiol
- E. Ibuprofen
- F. Tamoxifen

Not required right now, we will take it in pharmacology

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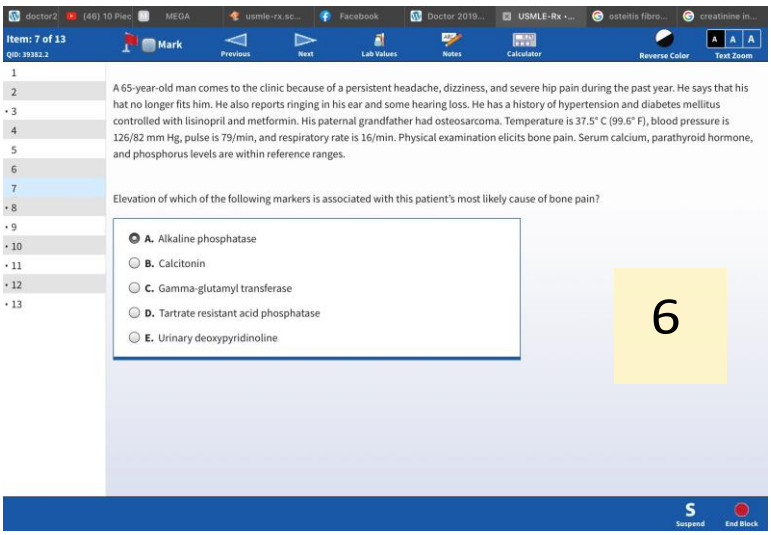

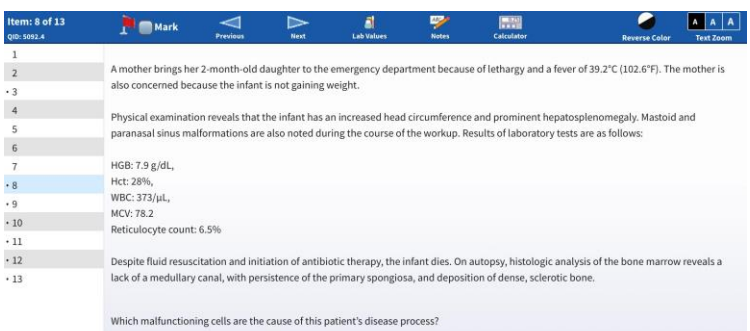

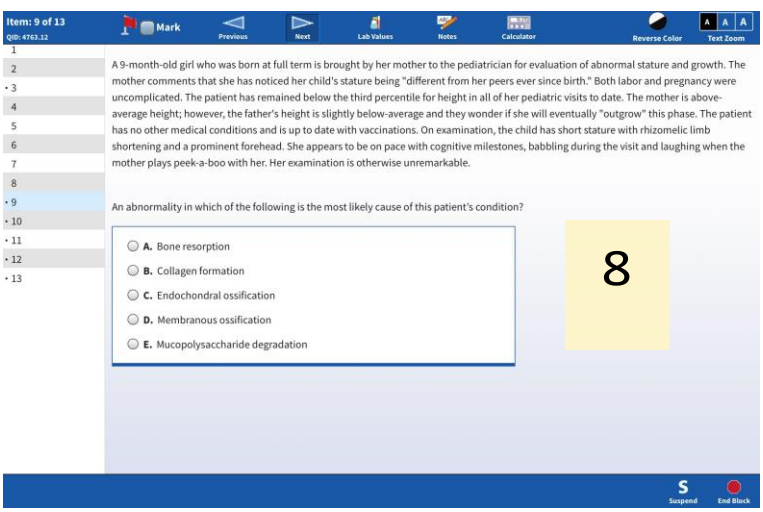

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A 2-year-old girl is brought to the clinic by her adoptive parents for a well-child examination. The patient's parents do not know the detailed medical history of her biological parents. Her height is below the second percentile, and her weight is below the third percentile. On examination, the patient appears to have a normal trunk size, but her head appears large and her arms and legs appear short. The remainder of the examination findings are within normal limits.

Which of the following is associated with this condition?

- **A.** Advanced maternal age
- **B.** Advanced paternal age
- **C.** Growth hormone deficiency
- **D.** Iodine deficiency in utero
- **E.** Thalidomide exposure in utero

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QID: 2616.14

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A 2-month-old, full-term boy is brought to the clinic by his parents for a well-child visit. He is breastfeeding well and gaining weight adequately. He is producing the appropriate amount of wet diapers and bowel movements per day. He coos and smiles during the visit but is unable to hold his head up. It is found upon physical examination that he has a large head with a prominent forehead, a long, narrow trunk, and short extremities, especially in the proximal segments. The growth chart shows significantly short stature for his age group.

Which of the following processes is most likely defective in this child's disorder?

- **A.** Defective osteoclast resorption
- **B.** Excessive resorption of cartilage
- **C.** Mineralization of cartilaginous growth plates
- **D.** Production of hyaline cartilage models
- **E.** Secretion of osteoid by osteoblasts without a hyaline cartilage model

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An 87-year-old woman visits her primary care physician for a routine physical examination. She has a history of compression fractures secondary to minor trauma and most recently sustained a wrist fracture when she fell while bathing. She has a 35–pack-year history of smoking but quit 25 years ago. The patient has no new symptoms but reports increasing stiffness and joint pain. After noting reduced mobility in her previously affected joints, her physician orders x-ray studies that reveal cortical thinning and increased radiolucency.

Choice	Calcium	Phosphorus	Alkaline phosphatase	Magnesium
A	↓	↑	↑	normal
B	normal	normal	normal	normal
C	normal	normal	↑	normal
D	↑	↓	↑	normal
E	↑	↑	↑	normal

11

What changes in calcium, phosphorus, alkaline phosphatase, and magnesium levels, as listed in the table, would be expected?

- **A.** A
- **B.** B
- **C.** C
- **D.** D
- **E.** E

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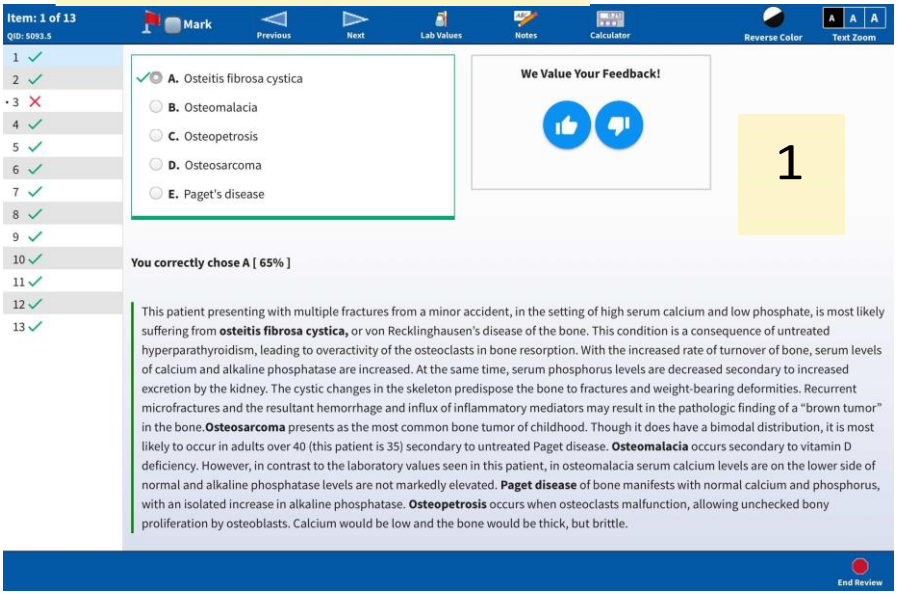
Answers


Item: 1 of 13
QID: 5093.5
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Lab Values
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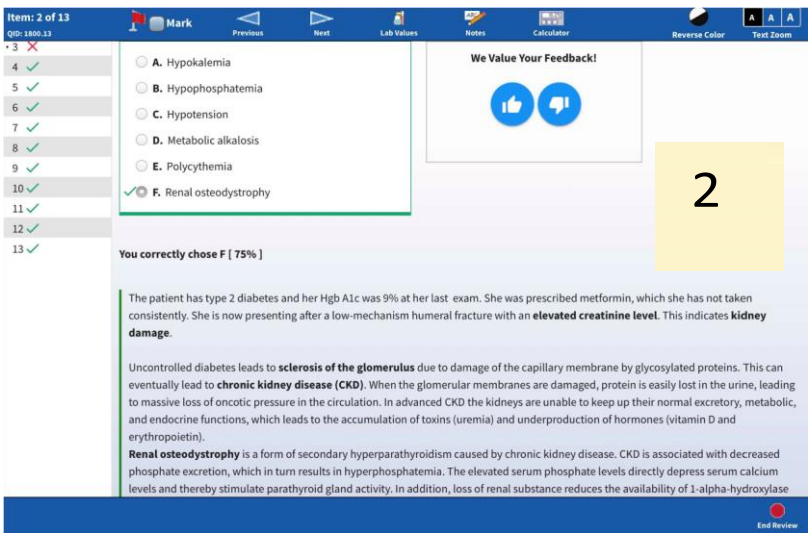
Text Zoom
A. Osteitis fibrosa cystica
B. Osteomalacia
C. Osteopetrosis
D. Osteosarcoma
E. Paget's disease
We Value Your Feedback!
1
You correctly chose A [65%]
This patient presenting with multiple fractures from a minor accident, in the setting of high serum calcium and low phosphate, is most likely suffering from osteitis fibrosa cystica, or von Recklinghausen's disease of the bone. This condition is a consequence of untreated hyperparathyroidism, leading to overactivity of the osteoclasts in bone resorption. With the increased rate of turnover of bone, serum levels of calcium and alkaline phosphatase are increased. At the same time, serum phosphorus levels are decreased secondary to increased excretion by the kidney. The cystic changes in the skeleton predispose the bone to fractures and weight-bearing deformities. Recurrent microfractures and the resultant hemorrhage and influx of inflammatory mediators may result in the pathologic finding of a "brown tumor" in the bone.Osteosarcoma presents as the most common bone tumor of childhood. Though it does have a bimodal distribution, it is most likely to occur in adults over 40 (this patient is 35) secondary to untreated Paget disease. Osteomalacia occurs secondary to vitamin D deficiency. However, in contrast to the laboratory values seen in this patient, in osteomalacia serum calcium levels are on the lower side of normal and alkaline phosphatase levels are not markedly elevated. Paget disease of bone manifests with normal calcium and phosphorus, with an isolated increase in alkaline phosphatase. Osteopetrosis occurs when osteoclasts malfunction, allowing unchecked bony proliferation by osteoblasts. Calcium would be low and the bone would be thick, but brittle.
End Review


Item: 2 of 13
QID: 1800.13
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Lab Values
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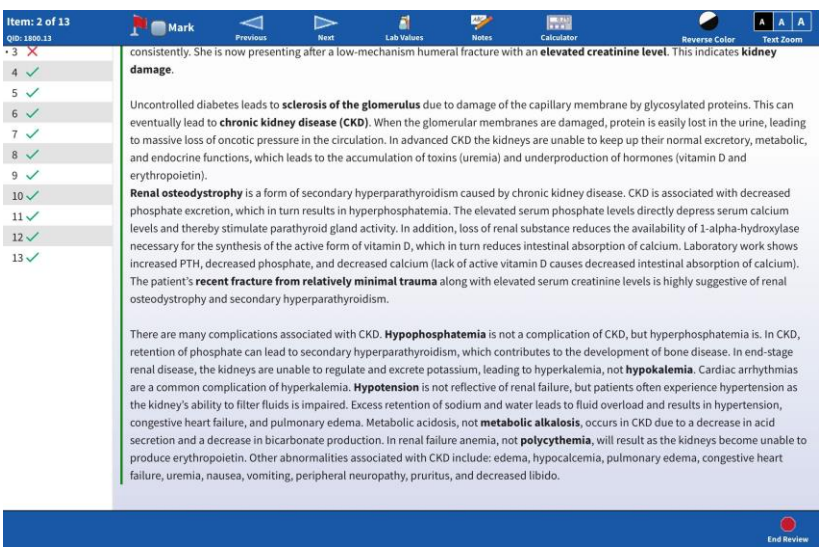
Text Zoom
A. Hypokalemia
B. Hypophosphatemia
C. Hypotension
D. Metabolic alkalosis
E. Polycythemia
F. Renal osteodystrophy
We Value Your Feedback!
2
You correctly chose F [75%]
The patient has type 2 diabetes and her Hgb A1c was 9% at her last exam. She was prescribed metformin, which she has not taken consistently. She is now presenting after a low-mechanism humeral fracture with an elevated creatinine level. This indicates kidney damage.
Uncontrolled diabetes leads to sclerosis of the glomerulus due to damage of the capillary membrane by glycosylated proteins. This can eventually lead to chronic kidney disease (CKD). When the glomerular membranes are damaged, protein is easily lost in the urine, leading to massive loss of oncotic pressure in the circulation. In advanced CKD the kidneys are unable to keep up their normal excretory, metabolic, and endocrine functions, which leads to the accumulation of toxins (uremia) and underproduction of hormones (vitamin D and erythropoietin).
Renal osteodystrophy is a form of secondary hyperparathyroidism caused by chronic kidney disease. CKD is associated with decreased phosphate excretion, which in turn results in hyperphosphatemia. The elevated serum phosphate levels directly depress serum calcium levels and thereby stimulate parathyroid gland activity. In addition, loss of renal substance reduces the availability of 1-alpha-hydroxylase
End Review


Item: 2 of 13
QID: 1800.13
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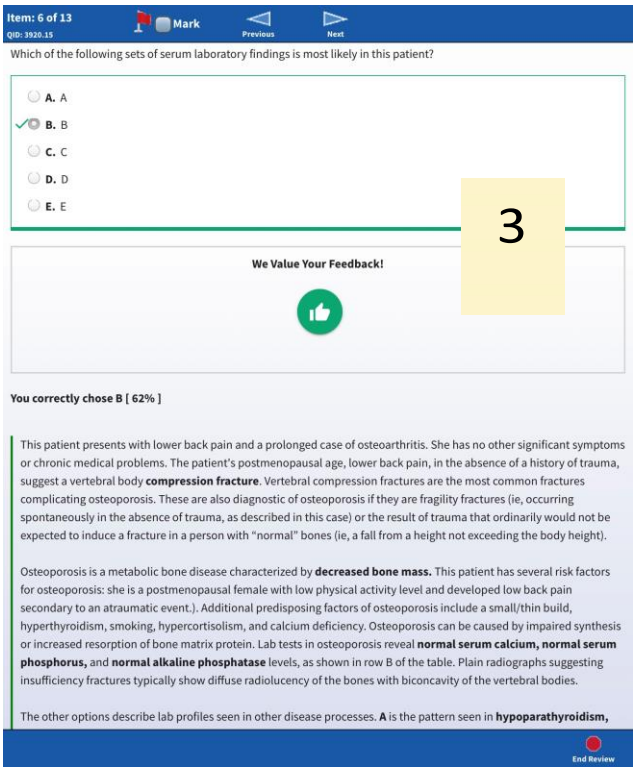
Uncontrolled diabetes leads to sclerosis of the glomerulus due to damage of the capillary membrane by glycosylated proteins. This can eventually lead to chronic kidney disease (CKD). When the glomerular membranes are damaged, protein is easily lost in the urine, leading to massive loss of oncotic pressure in the circulation. In advanced CKD the kidneys are unable to keep up their normal excretory, metabolic, and endocrine functions, which leads to the accumulation of toxins (uremia) and underproduction of hormones (vitamin D and erythropoietin).
Renal osteodystrophy is a form of secondary hyperparathyroidism caused by chronic kidney disease. CKD is associated with decreased phosphate excretion, which in turn results in hyperphosphatemia. The elevated serum phosphate levels directly depress serum calcium levels and thereby stimulate parathyroid gland activity. In addition, loss of renal substance reduces the availability of 1-alpha-hydroxylase necessary for the synthesis of the active form of vitamin D, which in turn reduces intestinal absorption of calcium. Laboratory work shows increased PTH, decreased phosphate, and decreased calcium (lack of active vitamin D causes decreased intestinal absorption of calcium). The patient's recent fracture from relatively minimal trauma along with elevated serum creatinine levels is highly suggestive of renal osteodystrophy and secondary hyperparathyroidism.
There are many complications associated with CKD. Hypophosphatemia is not a complication of CKD, but hyperphosphatemia is. In CKD, retention of phosphate can lead to secondary hyperparathyroidism, which contributes to the development of bone disease. In end-stage renal disease, the kidneys are unable to regulate and excrete potassium, leading to hyperkalemia, not hypokalemia. Cardiac arrhythmias are a common complication of hyperkalemia. Hypotension is not reflective of renal failure, but patients often experience hypertension as the kidney's ability to filter fluids is impaired. Excess retention of sodium and water leads to fluid overload and results in hypertension, congestive heart failure, and pulmonary edema. Metabolic acidosis, not metabolic alkalosis, occurs in CKD due to a decrease in acid secretion and a decrease in bicarbonate production. In renal failure anemia, not polycythemia, will result as the kidneys become unable to produce erythropoietin. Other abnormalities associated with CKD include: edema, hypocalcemia, pulmonary edema, congestive heart failure, uremia, nausea, vomiting, peripheral neuropathy, pruritus, and decreased libido.
End Review



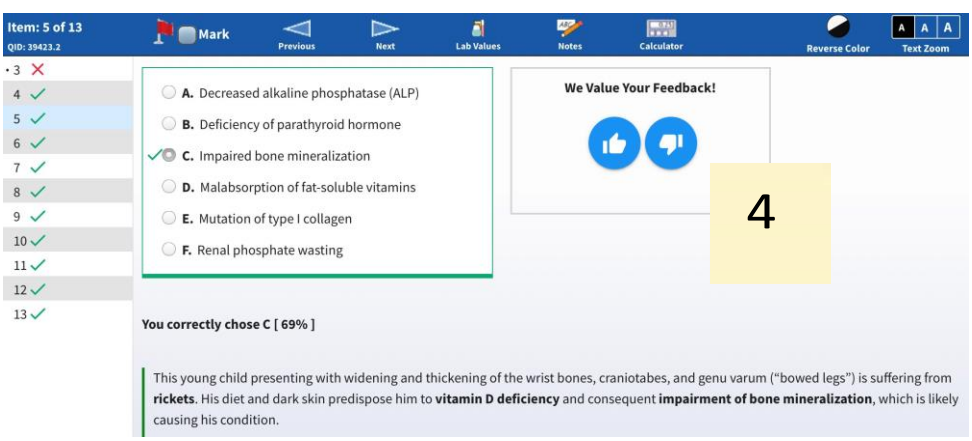
You correctly chose B [62%]

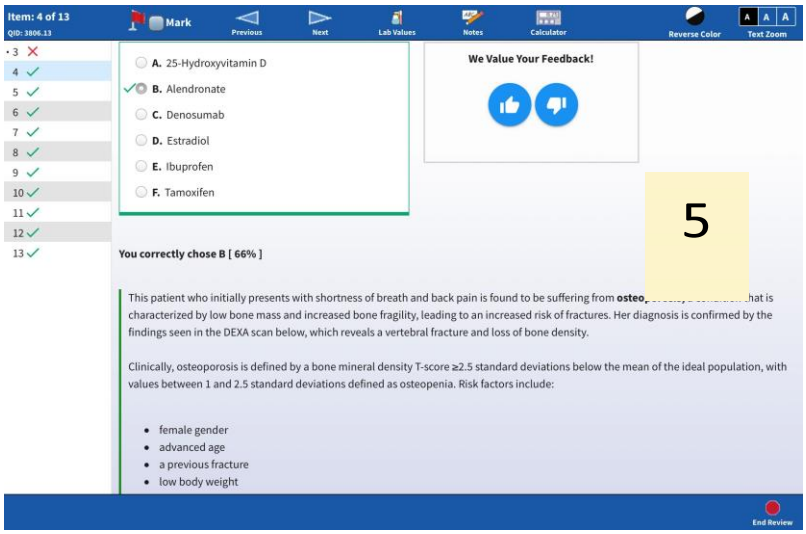
This patient presents with lower back pain and a prolonged case of osteoarthritis. She has no other significant symptoms or chronic medical problems. The patient's postmenopausal age, lower back pain, in the absence of a history of trauma, suggest a vertebral body **compression fracture**. Vertebral compression fractures are the most common fractures complicating osteoporosis. These are also diagnostic of osteoporosis if they are fragility fractures (ie, occurring spontaneously in the absence of trauma, as described in this case) or the result of trauma that ordinarily would not be expected to induce a fracture in a person with "normal" bones (ie, a fall from a height not exceeding the body height).

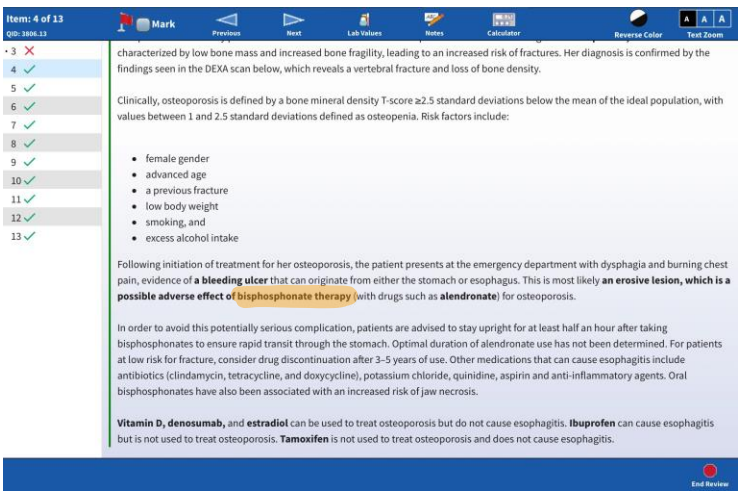
Osteoporosis is a metabolic bone disease characterized by **decreased bone mass.** This patient has several risk factors for osteoporosis: she is a postmenopausal female with low physical activity level and developed low back pain secondary to an atraumatic event.). Additional predisposing factors of osteoporosis include a small/thin build, hyperthyroidism, smoking, hypercortisolism, and calcium deficiency. Osteoporosis can be caused by impaired synthesis or increased resorption of bone matrix protein. Lab tests in osteoporosis reveal **normal serum calcium, normal serum phosphorus,** and **normal alkaline phosphatase** levels, as shown in row B of the table. Plain radiographs suggesting insufficiency fractures typically show diffuse radiolucency of the bones with biconcavity of the vertebral bodies.

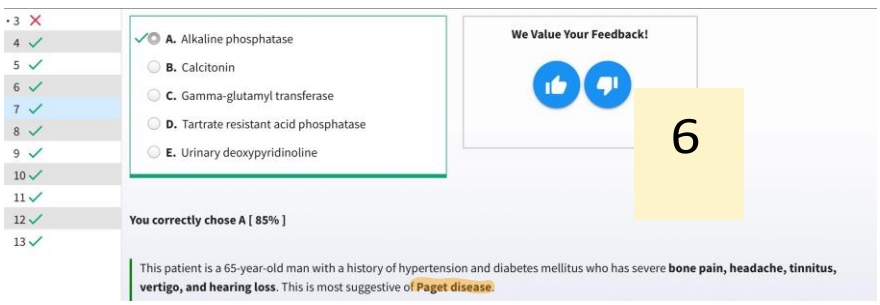
The other options describe lab profiles seen in other disease processes. **A** is the pattern seen in **hypoparathyroidism,** which most commonly manifests with symptoms of hypocalcemia: tetany, depression, dementia, and seizures. These are not seen in this patient. **C** is the pattern for **Paget disease.** While this patient has some features of Paget disease (eg, bone pain and fractures), the radiograph does not demonstrate the abnormal bone architecture pattern seen in this condition. **D** is the laboratory pattern for **hyperparathyroidism,** which typically manifests with the symptoms of hypercalcemia: kidney stones, polyuria, constipation, abdominal pain, depression, and psychosis. While this patient does have osteopenia, the patient has no additional symptoms or risk factors suggestive of hyperparathyroidism. Alkaline phosphatase is often increased in diseases with increased osteoblast activity and bone remodeling, such as Paget disease and hyperparathyroidism. **E** is the laboratory pattern for **osteomalacia/rickets disease** which presents with signs of hypocalcemic tetany which is not described in this patient's presentation.

End Review

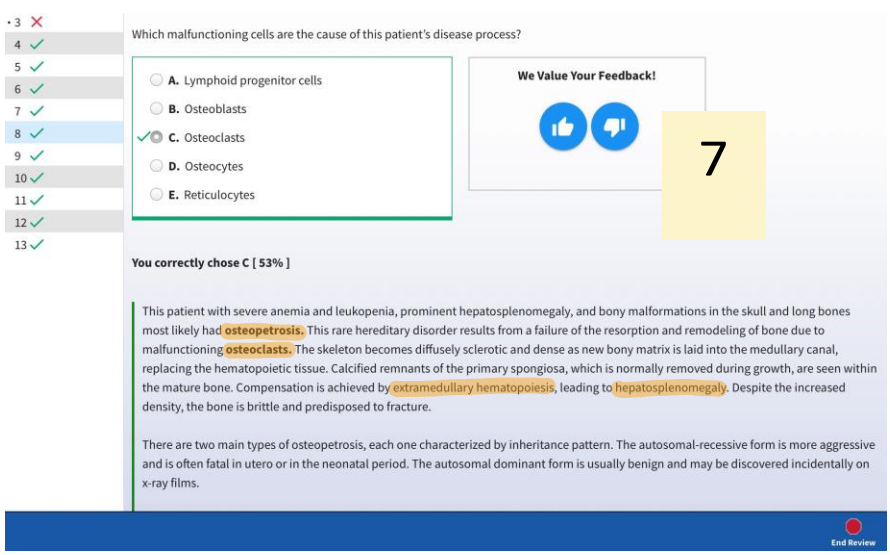


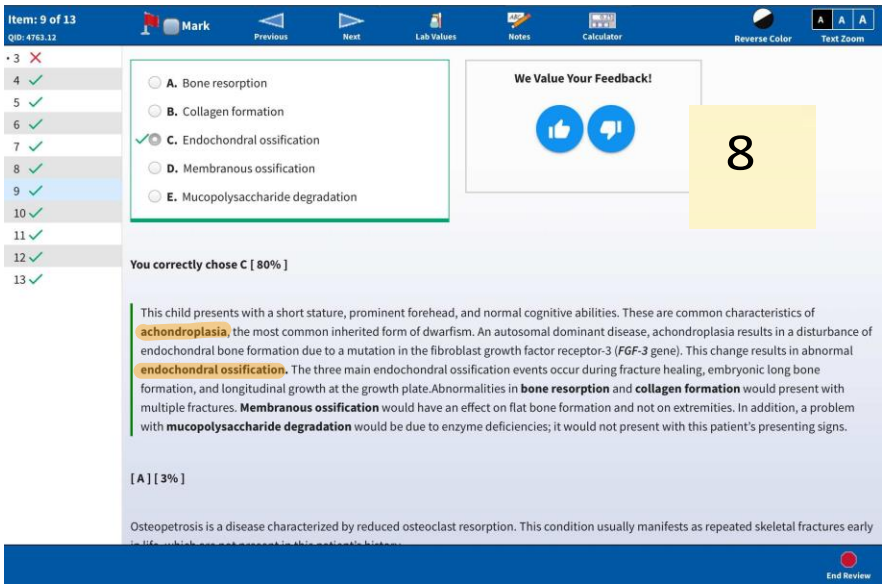






When evaluating for Paget disease, serum phosphate, calcium, and parathyroid hormone will be within reference ranges with an **increased alkaline phosphatase (ALP)** concentration**.** An increased ALP concentration is the result of increased osteoblastic activity, as described above. Notably, increased ALP concentrations can be seen in cholestasis, obstructive biliary diseases, osteosarcoma, or metastasis to bone (commonly from prostate cancer).




Item: 9 of 13
QID: 4763.12
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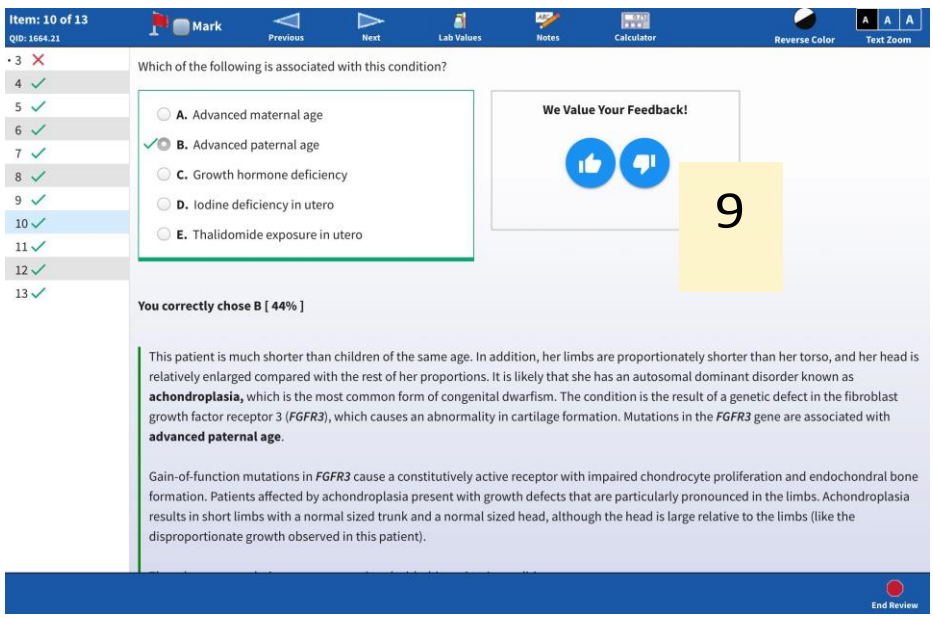
A. Bone resorption
B. Collagen formation
C. Endochondral ossification
D. Membranous ossification
E. Mucopolysaccharide degradation
We Value Your Feedback!
8
You correctly chose C [80%]
This child presents with a short stature, prominent forehead, and normal cognitive abilities. These are common characteristics of achondroplasia, the most common inherited form of dwarfism. An autosomal dominant disease, achondroplasia results in a disturbance of endochondral bone formation due to a mutation in the fibroblast growth factor receptor-3 (FGF-3 gene). This change results in abnormal endochondral ossification. The three main endochondral ossification events occur during fracture healing, embryonic long bone formation, and longitudinal growth at the growth plate.Abnormalities in bone resorption and collagen formation would present with multiple fractures. Membranous ossification would have an effect on flat bone formation and not on extremities. In addition, a problem with mucopolysaccharide degradation would be due to enzyme deficiencies; it would not present with this patient's presenting signs.
[A] [3%]
Osteopetrosis is a disease characterized by reduced osteoclast resorption. This condition usually manifests as repeated skeletal fractures early
End Review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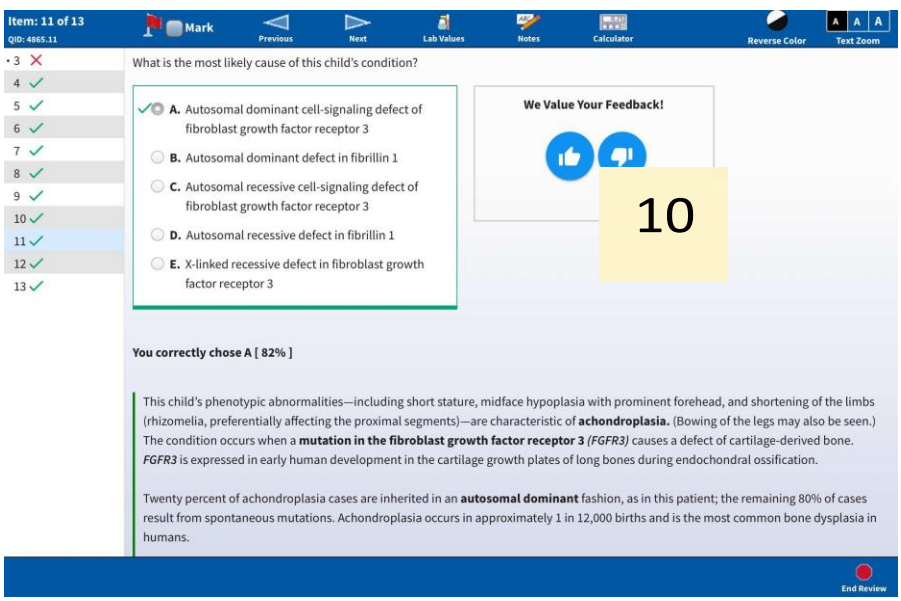
Which of the following is associated with this condition?
A. Advanced maternal age
B. Advanced paternal age
C. Growth hormone deficiency
D. Iodine deficiency in utero
E. Thalidomide exposure in utero
We Value Your Feedback!
9
You correctly chose B [44%]
This patient is much shorter than children of the same age. In addition, her limbs are proportionately shorter than her torso, and her head is relatively enlarged compared with the rest of her proportions. It is likely that she has an autosomal dominant disorder known as achondroplasia, which is the most common form of congenital dwarfism. The condition is the result of a genetic defect in the fibroblast growth factor receptor 3 (FGFR3), which causes an abnormality in cartilage formation. Mutations in the FGFR3 gene are associated with advanced paternal age.
Gain-of-function mutations in FGFR3 cause a constitutively active receptor with impaired chondrocyte proliferation and endochondral bone formation. Patients affected by achondroplasia present with growth defects that are particularly pronounced in the limbs. Achondroplasia results in short limbs with a normal sized trunk and a normal sized head, although the head is large relative to the limbs (like the disproportionate growth observed in this patient).
End Review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QID: 4865.11
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What is the most likely cause of this child's condition?
A. Autosomal dominant cell-signaling defect of fibroblast growth factor receptor 3
B. Autosomal dominant defect in fibrillin 1
C. Autosomal recessive cell-signaling defect of fibroblast growth factor receptor 3
D. Autosomal recessive defect in fibrillin 1
E. X-linked recessive defect in fibroblast growth factor receptor 3
We Value Your Feedback!
10
You correctly chose A [82%]
This child's phenotypic abnormalities—including short stature, midface hypoplasia with prominent forehead, and shortening of the limbs (rhizomelia, preferentially affecting the proximal segments)—are characteristic of achondroplasia. (Bowing of the legs may also be seen.) The condition occurs when a mutation in the fibroblast growth factor receptor 3 (FGFR3) causes a defect of cartilage-derived bone. FGFR3 is expressed in early human development in the cartilage growth plates of long bones during endochondral ossification.
Twenty percent of achondroplasia cases are inherited in an autosomal dominant fashion, as in this patient; the remaining 80% of cases result from spontaneous mutations. Achondroplasia occurs in approximately 1 in 12,000 births and is the most common bone dysplasia in humans.
End Review

- A. A
- ✓ B. B
- C. C
- D. D
- E. E

11

We Value Your Feedback!

You correctly chose B [62%]

This patient's sex, age, smoking status, and history of fractures are strongly suggestive of **osteoporosis.** Osteoporosis is characterized by loss of trabecular and cortical bone mass and is most commonly due to increased bone resorption related to decreased estrogen production and aging. The x-ray shows diffuse radiolucency of bones with biconcavity of the vertebral bodies, caused by insufficiency fractures that occurred due to osteoporosis.

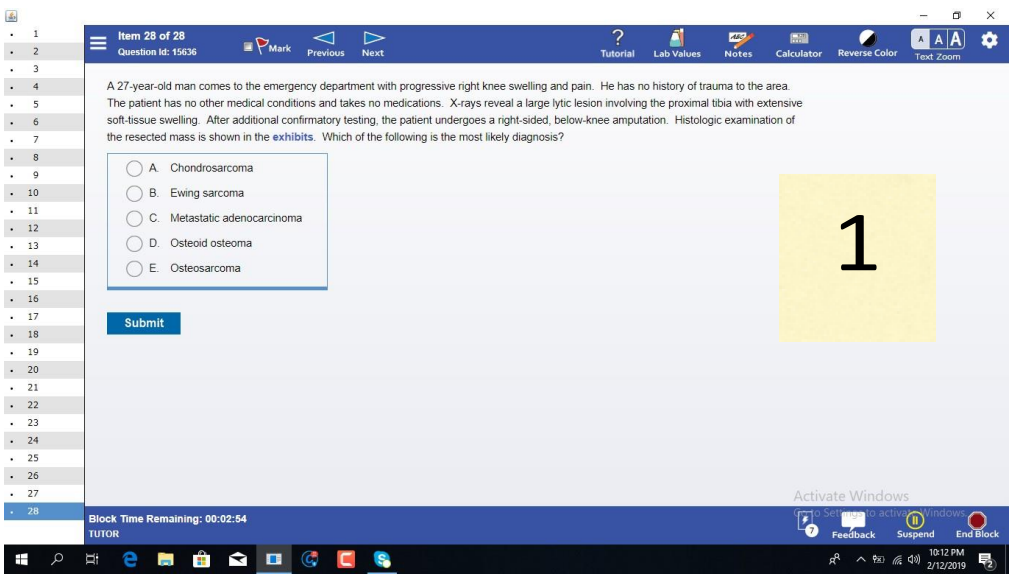
Gross metabolic abnormalities are not characteristic of osteoporosis. Most patients with osteoporosis do not demonstrate any laboratory abnormalities. Decreased bone mass does not occur as the result of abnormal levels of vitamins, minerals, or hormones but is due to an imbalance in the activity of osteoblasts and osteoclasts. This imbalance can be caused by age-related changes, genetic factors, and in women, postmenopausal states. Bone pain and fractures in the context of laboratory abnormalities are suggestive of alternative pathologies.

Low calcium and high phosphate levels are suggestive of secondary hyperparathyroidism with **excessively elevated parathyroid hormone** (PTH), usually caused by renal insufficiency. **An isolated increase in alkaline phosphatase** (ALP) is seen in patients with Paget disease of bone. **Increased calcium and decreased phosphate** are suggestive of primary hyperparathyroidism, with **elevated PTH** (ALP may also be elevated). **Elevated calcium and elevated alkaline phosphatase** can indicate bone metastasis. The most common primary cancers that metastasize to bone include breast, prostate, lung, kidney, and thyroid cancers.

MSS

6 USMLE QUESTIONS
(UWORLD + RX)
With clarifications

4th and 5th lecture of pathology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Question Id: 15636
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A 27-year-old man comes to the emergency department with progressive right knee swelling and pain. He has no history of trauma to the area. The patient has no other medical conditions and takes no medications. X-rays reveal a large lytic lesion involving the proximal tibia with extensive soft-tissue swelling. After additional confirmatory testing, the patient undergoes a right-sided, below-knee amputation. Histologic examination of the resected mass is shown in the exhibits. Which of the following is the most likely diagnosis?
A. Chondrosarcoma
B. Ewing sarcoma
C. Metastatic adenocarcinoma
D. Osteoid osteoma
E. Osteosarcoma
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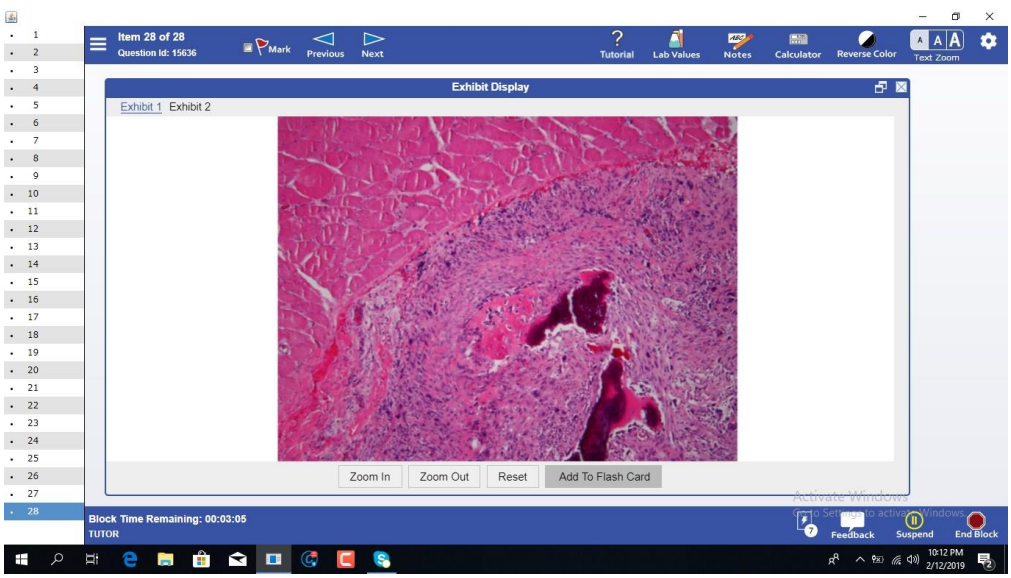
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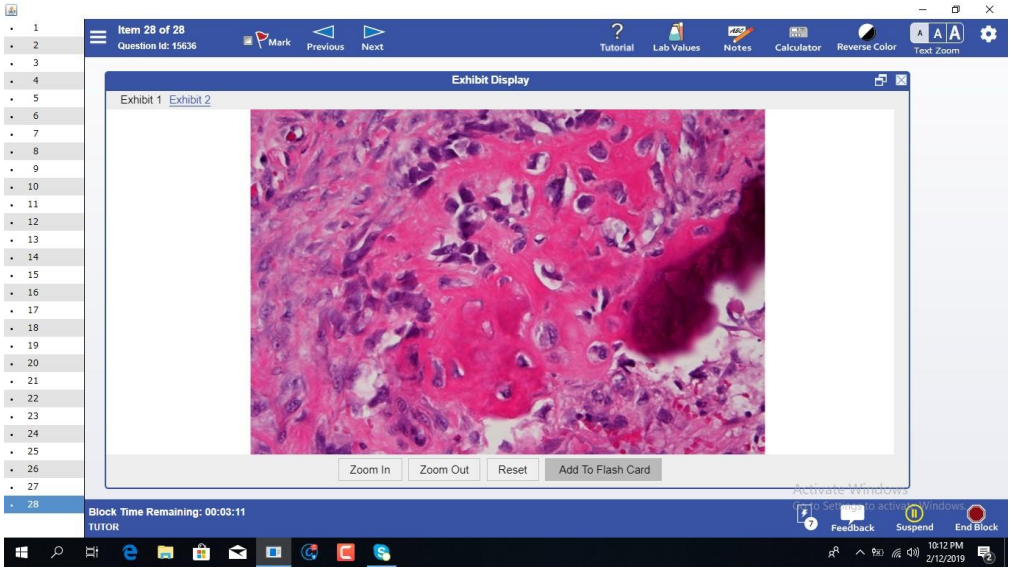
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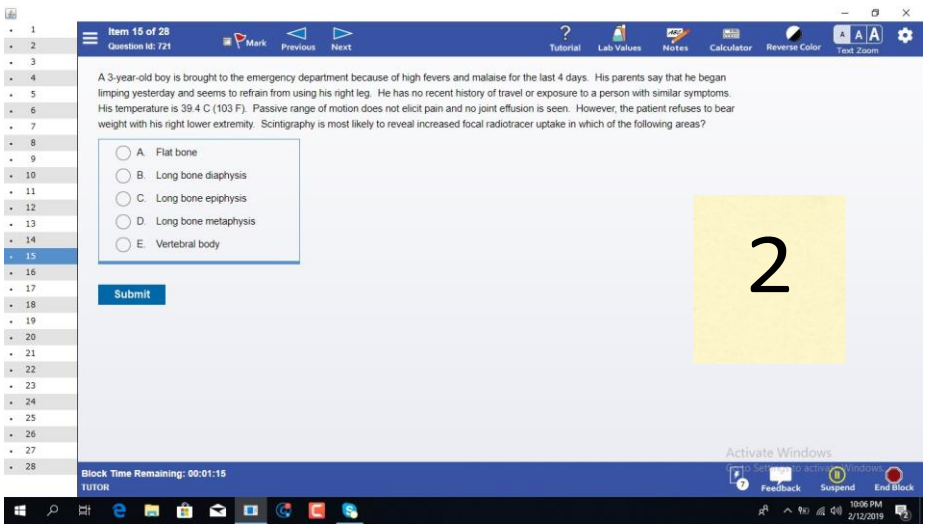
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Question Id: 721
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A 3-year-old boy is brought to the emergency department because of high fevers and malaise for the last 4 days. His parents say that he began limping yesterday and seems to refrain from using his right leg. He has no recent history of travel or exposure to a person with similar symptoms. His temperature is 39.4 C (103 F). Passive range of motion does not elicit pain and no joint effusion is seen. However, the patient refuses to bear weight with his right lower extremity. Scintigraphy is most likely to reveal increased focal radiotracer uptake in which of the following areas?
A. Flat bone
B. Long bone diaphysis
C. Long bone epiphysis
D. Long bone metaphysis
E. Vertebral body
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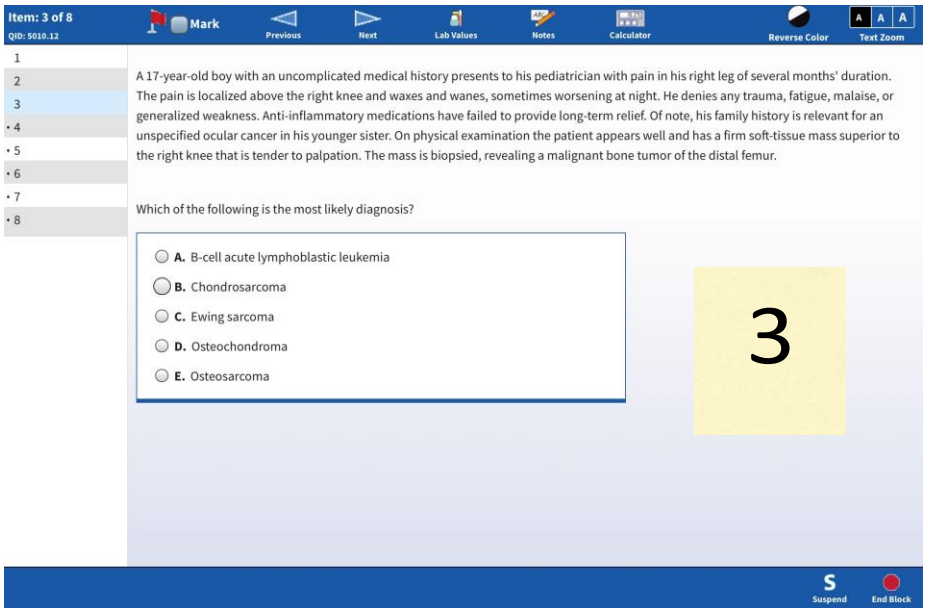
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A 17-year-old boy with an uncomplicated medical history presents to his pediatrician with pain in his right leg of several months' duration. The pain is localized above the right knee and waxes and wanes, sometimes worsening at night. He denies any trauma, fatigue, malaise, or generalized weakness. Anti-inflammatory medications have failed to provide long-term relief. Of note, his family history is relevant for an unspecified ocular cancer in his younger sister. On physical examination the patient appears well and has a firm soft-tissue mass superior to the right knee that is tender to palpation. The mass is biopsied, revealing a malignant bone tumor of the distal femur.
Which of the following is the most likely diagnosis?
A. B-cell acute lymphoblastic leukemia
B. Chondrosarcoma
C. Ewing sarcoma
D. Osteochondroma
E. Osteosarcoma
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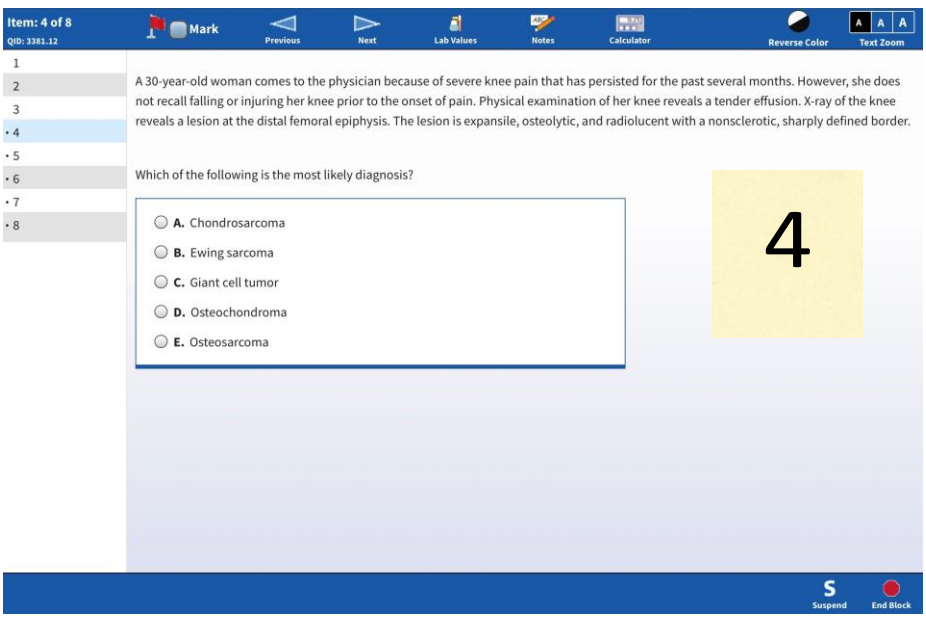
Item: 4 of 8
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A 30-year-old woman comes to the physician because of severe knee pain that has persisted for the past several months. However, she does not recall falling or injuring her knee prior to the onset of pain. Physical examination of her knee reveals a tender effusion. X-ray of the knee reveals a lesion at the distal femoral epiphysis. The lesion is expansile, osteolytic, and radiolucent with a nonsclerotic, sharply defined border.
Which of the following is the most likely diagnosis?
A. Chondrosarcoma
B. Ewing sarcoma
C. Giant cell tumor
D. Osteochondroma
E. Osteosarcoma
4
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Item: 6 of 8
QID: 1261.14
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A 40-year-old woman comes to the gynecologist after finding a lump in her right breast during a monthly self-examination. The patient was treated for adrenocortical cancer 18 months earlier. The patient's older sister, who just turned 45, was recently diagnosed with breast cancer. Additionally, her 29-year-old brother was diagnosed with osteosarcoma as a child, her 37-year-old sister was diagnosed with ovarian cancer 2 years ago and leukemia 4 years ago. Her father was also diagnosed with leukemia. Mammography confirms the presence of a mass of 3.2-cm density with irregular margins in the right breast. The gynecologist orders a biopsy of the mass and a section of the tissue is shown.

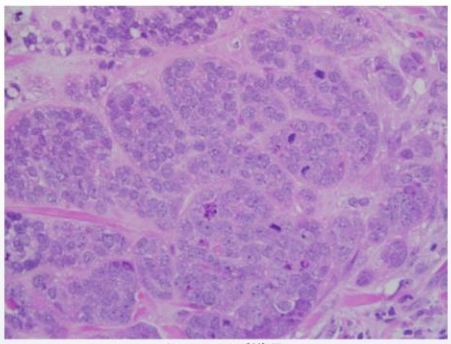

Image courtesy of Difu Wu

5

The increased susceptibility to cancer in this family is caused by a mutation in which of the following genes?

- **A.** *APC*
- **B.** *BRCA1*
- **C.** *BRCA2*
- **D.** *RET*
- **E.** p53

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A 70-year-old woman sustains a fracture to the left femoral head after a fall.

Injury to which of the following arteries increases the risk of osteonecrosis in this patient?

- **A.** Deep femoral artery
- **B.** Inferior gluteal artery
- **D.** Medial femoral circumflex artery
- **E.** Obturator artery

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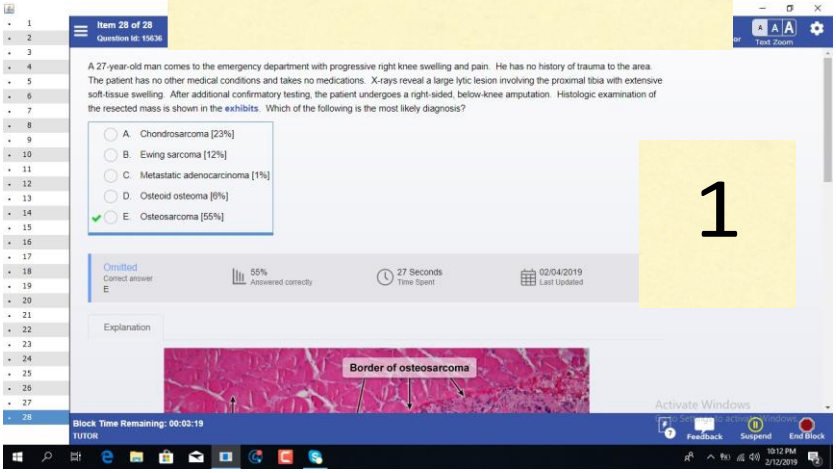
Answers


Item 28 of 28
Question Id: 15636
A 27-year-old man comes to the emergency department with progressive right knee swelling and pain. He has no history of trauma to the area. The patient has no other medical conditions and takes no medications. X-rays reveal a large lytic lesion involving the proximal tibia with extensive soft-tissue swelling. After additional confirmatory testing, the patient undergoes a right-sided, below-knee amputation. Histologic examination of the resected mass is shown in the exhibits. Which of the following is the most likely diagnosis?
A. Chondrosarcoma [23%]
B. Ewing sarcoma [12%]
C. Metastatic adenocarcinoma [1%]
D. Osteoid osteoma [6%]
E. Osteosarcoma [55%]
Omitted
Correct answer
E
55%
Answered correctly
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Explanation
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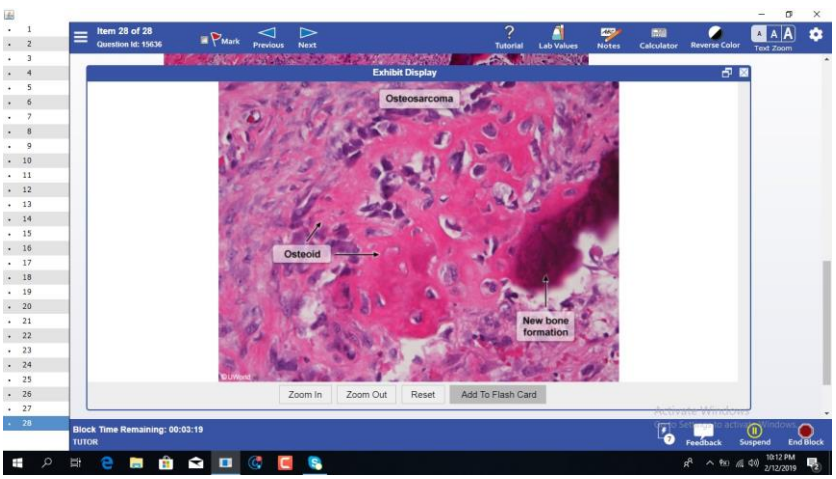
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Osteosarcoma
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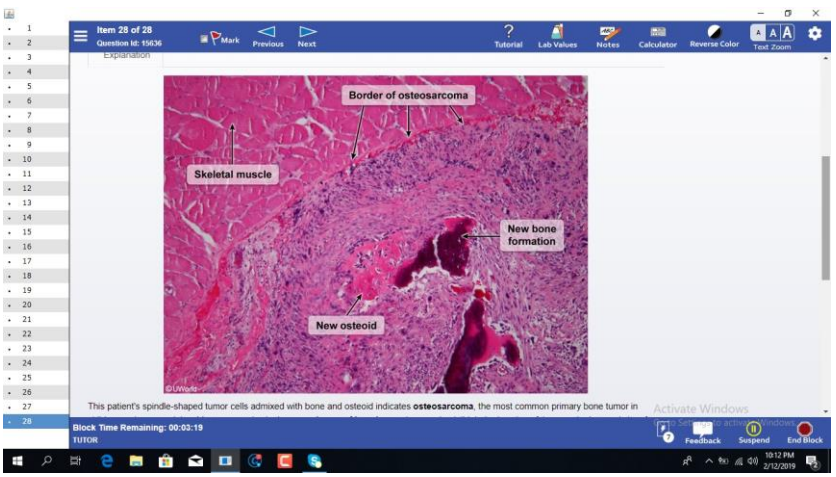
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Explanation
Border of osteosarcoma
Skeletal muscle
New bone formation
New osteoid
This patient's spindle-shaped tumor cells admixed with bone and osteoid indicates osteosarcoma, the most common primary bone tumor in
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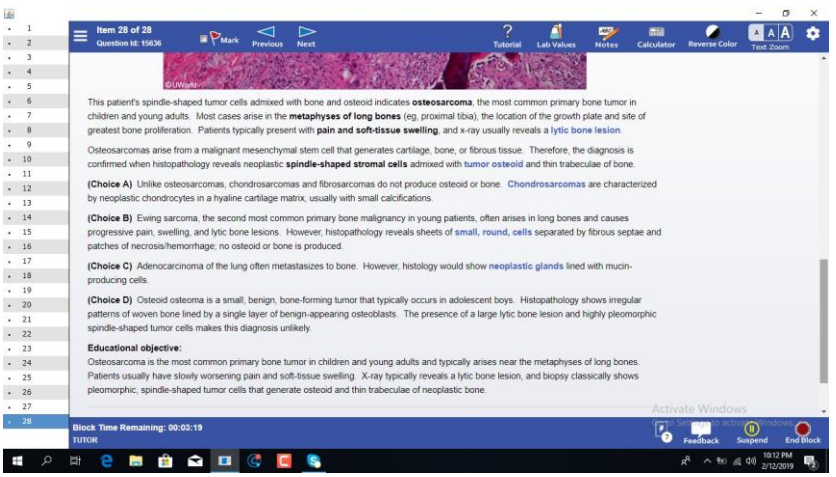
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This patient's spindle-shaped tumor cells admixed with bone and osteoid indicates osteosarcoma, the most common primary bone tumor in children and young adults. Most cases arise in the metaphyses of long bones (eg, proximal tibia), the location of the growth plate and site of greatest bone proliferation. Patients typically present with pain and soft-tissue swelling, and x-ray usually reveals a lytic bone lesion.
Osteosarcomas arise from a malignant mesenchymal stem cell that generates cartilage, bone, or fibrous tissue. Therefore, the diagnosis is confirmed when histopathology reveals neoplastic spindle-shaped stromal cells admixed with tumor osteoid and thin trabeculae of bone.
(Choice A) Unlike osteosarcomas, chondrosarcomas and fibrosarcomas do not produce osteoid or bone. Chondrosarcomas are characterized by neoplastic chondrocytes in a hyaline cartilage matrix, usually with small calcifications.
(Choice B) Ewing sarcoma, the second most common primary bone malignancy in young patients, often arises in long bones and causes progressive pain, swelling, and lytic bone lesions. However, histopathology reveals sheets of small, round, cells separated by fibrous septae and patches of necrosis/hemorrhage; no osteoid or bone is produced.
(Choice C) Adenocarcinoma of the lung often metastasizes to bone. However, histology would show neoplastic glands lined with mucin-producing cells.
(Choice D) Osteoid osteoma is a small, benign, bone-forming tumor that typically occurs in adolescent boys. Histopathology shows irregular patterns of woven bone lined by a single layer of benign-appearing osteoblasts. The presence of a large lytic bone lesion and highly pleomorphic spindle-shaped tumor cells makes this diagnosis unlikely.
Educational objective:
Osteosarcoma is the most common primary bone tumor in children and young adults and typically arises near the metaphyses of long bones. Patients usually have slowly worsening pain and soft-tissue swelling. X-ray typically reveals a lytic bone lesion, and biopsy classically shows pleomorphic, spindle-shaped tumor cells that generate osteoid and thin trabeculae of neoplastic bone.
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Question Id: 721

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A 3-year-old boy is brought to the emergency department because of high fevers and malaise for the last 4 days. His parents say that he began limping yesterday and seems to refrain from using his right leg. He has no recent history of travel or exposure to a person with similar symptoms. His temperature is 39.4 C (103 F). Passive range of motion does not elicit pain and no joint effusion is seen. However, the patient refuses to bear weight with his right lower extremity. Scintigraphy is most likely to reveal increased focal radiotracer uptake in which of the following areas?

A. Flat bone [1%]
B. Long bone diaphysis [27%]
C. Long bone epiphysis [30%]
✔ D. Long bone metaphysis [39%]
E. Vertebral body [1%]

2

Omitted
Correct answer
D

39%
Answered correctly

4 Seconds
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Last Updated

Explanation

Progression of hematogenous osteomyelitis

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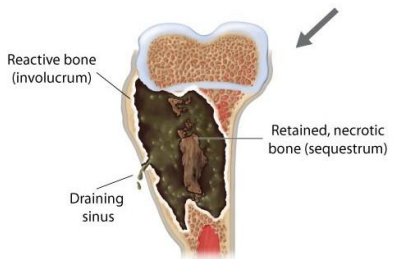
in focal bone marrow cellulitis

confined space compromises blood flow, causing necrosis

vascular channels into the cortex and spreads along periosteum



Development of chronic sequela

This patient most likely has hematogenous osteomyelitis, a disease that predominantly affects children, particularly boys. It usually affects the **metaphysis** of long bones, as this region contains slow-flowing, sinusoidal vasculature that is conducive to microbial passage. Adults are less likely to develop hematogenous osteomyelitis in the long bones due to changes associated with epiphysial closure.

Hematogenous osteomyelitis begins with a seeding event that causes an acute cellulitis of the bone marrow. The resulting inflammation within the confined boney space leads to increased intramedullary pressure, which compromises blood flow and forces infectious exudate through vascular

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This patient most likely has hematogenous osteomyelitis, a disease that predominantly affects children, particularly boys. It usually affects the **metaphysis** of long bones, as this region contains slow-flowing, sinusoidal vasculature that is conducive to microbial passage. Adults are less likely to develop hematogenous osteomyelitis in the long bones due to changes associated with epiphysial closure.

Hematogenous osteomyelitis begins with a seeding event that causes an acute cellulitis of the bone marrow. The resulting inflammation within the confined boney space leads to increased intramedullary pressure, which compromises blood flow and forces infectious exudate through vascular channels into the cortex and periosteal region. Disruption of the periosteal blood supply further contributes to bone ischemia, leading to necrosis. Without treatment, the infection can progress to chronic suppurative osteomyelitis, a condition in which necrotic bone (ie, sequestrum) serves as a reservoir for infection and becomes covered by a poorly constructed shell of new bone called an involucrum. One or more sinus tracts develop to drain the purulent material into the soft tissue or out to the skin surface. Proper treatment includes antibiotic therapy and debridement of necrotic bone.

(Choice A) Examples of flat bone are the skull, sternum, and bones of the pelvis. Osteomyelitis affecting the skull most commonly occurs via contiguous spread of infection from mastoiditis or dental abscess.

(Choice B) Ewing sarcoma typically arises in diaphysis of the long bones, especially the femur. It is the second most common malignant bone tumor in children after osteosarcoma. However, it occurs more frequently in older children (ages 10-15 years). Additionally, this patient's acute symptom onset and high-grade fever are more typical of an infectious process.

(Choice C) The long bone epiphysis is usually spared in osteomyelitis unless the acute infection is not treated. The infection could then spread into the epiphysis and adjacent joint, resulting in a pyogenic (septic) arthritis.

(Choice E) The **vertebral body** is the most common location for hematogenous osteomyelitis in **adults**. This is also the location of Pott disease, osteomyelitis of the vertebral body caused by *Mycobacterium tuberculosis*.

Educational objective:
Hematogenous osteomyelitis is most common in children and usually affects the metaphysis of long bones due to the slower blood flow and capillary fenestrae in this region. Without proper treatment, the infection can progress to chronic suppurative osteomyelitis.

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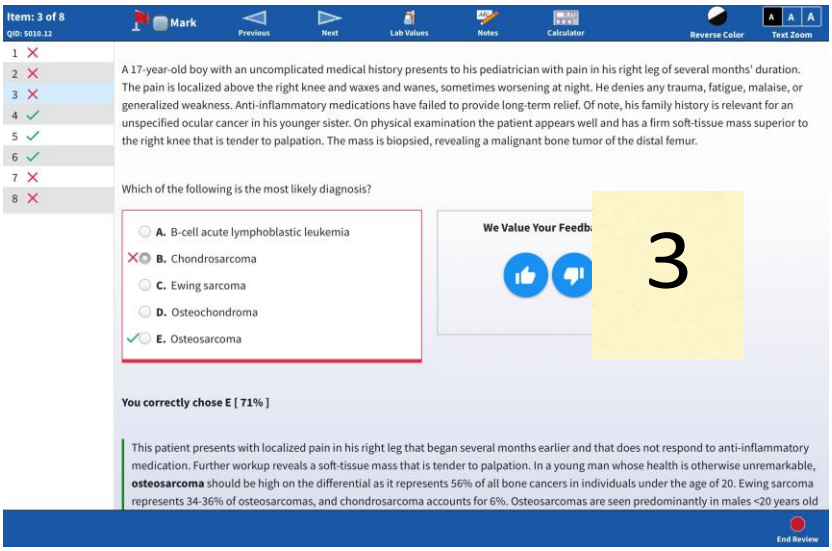
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A 17-year-old boy with an uncomplicated medical history presents to his pediatrician with pain in his right leg of several months' duration. The pain is localized above the right knee and waxes and wanes, sometimes worsening at night. He denies any trauma, fatigue, malaise, or generalized weakness. Anti-inflammatory medications have failed to provide long-term relief. Of note, his family history is relevant for an unspecified ocular cancer in his younger sister. On physical examination the patient appears well and has a firm soft-tissue mass superior to the right knee that is tender to palpation. The mass is biopsied, revealing a malignant bone tumor of the distal femur.
Which of the following is the most likely diagnosis?
A. B-cell acute lymphoblastic leukemia
B. Chondrosarcoma
C. Ewing sarcoma
D. Osteochondroma
E. Osteosarcoma
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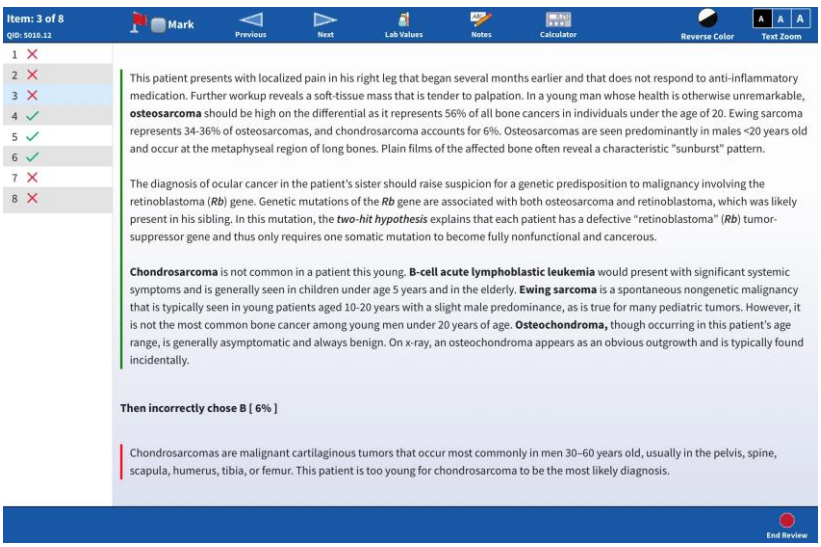
3
You correctly chose E [71%]
This patient presents with localized pain in his right leg that began several months earlier and that does not respond to anti-inflammatory medication. Further workup reveals a soft-tissue mass that is tender to palpation. In a young man whose health is otherwise unremarkable, osteosarcoma should be high on the differential as it represents 56% of all bone cancers in individuals under the age of 20. Ewing sarcoma represents 34-36% of osteosarcomas, and chondrosarcoma accounts for 6%. Osteosarcomas are seen predominantly in males <20 years old
End Review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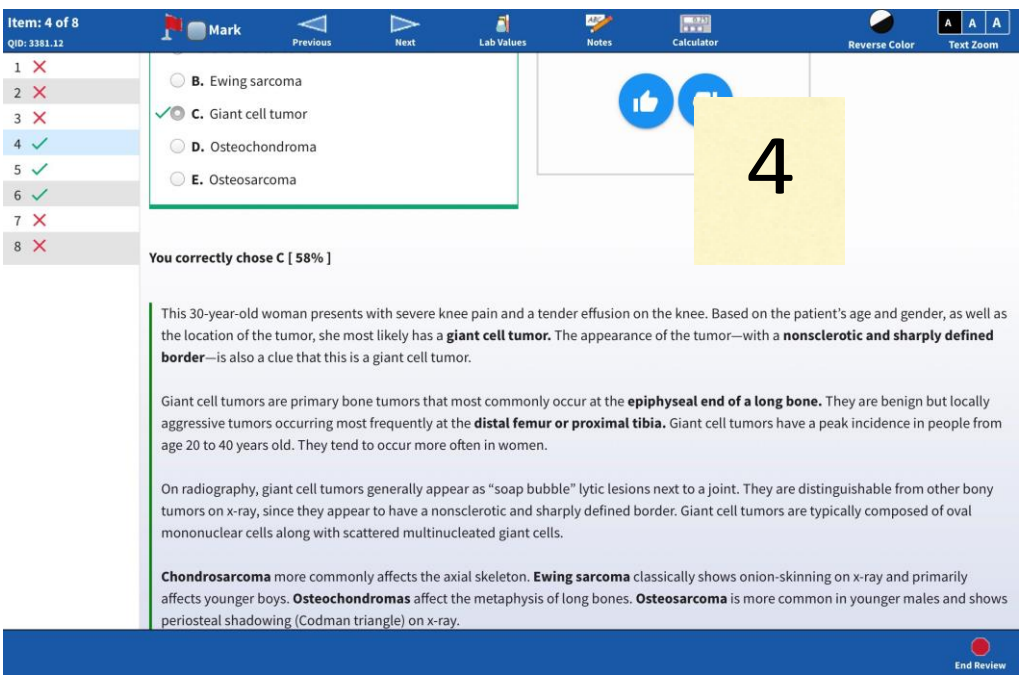
This patient presents with localized pain in his right leg that began several months earlier and that does not respond to anti-inflammatory medication. Further workup reveals a soft-tissue mass that is tender to palpation. In a young man whose health is otherwise unremarkable, osteosarcoma should be high on the differential as it represents 56% of all bone cancers in individuals under the age of 20. Ewing sarcoma represents 34-36% of osteosarcomas, and chondrosarcoma accounts for 6%. Osteosarcomas are seen predominantly in males <20 years old and occur at the metaphyseal region of long bones. Plain films of the affected bone often reveal a characteristic "sunburst" pattern.
The diagnosis of ocular cancer in the patient's sister should raise suspicion for a genetic predisposition to malignancy involving the retinoblastoma (Rb) gene. Genetic mutations of the Rb gene are associated with both osteosarcoma and retinoblastoma, which was likely present in his sibling. In this mutation, the two-hit hypothesis explains that each patient has a defective "retinoblastoma" (Rb) tumor-suppressor gene and thus only requires one somatic mutation to become fully nonfunctional and cancerous.
Chondrosarcoma is not common in a patient this young. B-cell acute lymphoblastic leukemia would present with significant systemic symptoms and is generally seen in children under age 5 years and in the elderly. Ewing sarcoma is a spontaneous nongenetic malignancy that is typically seen in young patients aged 10-20 years with a slight male predominance, as is true for many pediatric tumors. However, it is not the most common bone cancer among young men under 20 years of age. Osteochondroma, though occurring in this patient's age range, is generally asymptomatic and always benign. On x-ray, an osteochondroma appears as an obvious outgrowth and is typically found incidentally.
Then incorrectly chose B [6%]
Chondrosarcomas are malignant cartilaginous tumors that occur most commonly in men 30–60 years old, usually in the pelvis, spine, scapula, humerus, tibia, or femur. This patient is too young for chondrosarcoma to be the most likely diagnosis.
End Review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B. Ewing sarcoma
C. Giant cell tumor
D. Osteochondroma
E. Osteosarcoma
4
You correctly chose C [58%]
This 30-year-old woman presents with severe knee pain and a tender effusion on the knee. Based on the patient's age and gender, as well as the location of the tumor, she most likely has a giant cell tumor. The appearance of the tumor—with a nonsclerotic and sharply defined border—is also a clue that this is a giant cell tumor.
Giant cell tumors are primary bone tumors that most commonly occur at the epiphyseal end of a long bone. They are benign but locally aggressive tumors occurring most frequently at the distal femur or proximal tibia. Giant cell tumors have a peak incidence in people from age 20 to 40 years old. They tend to occur more often in women.
On radiography, giant cell tumors generally appear as "soap bubble" lytic lesions next to a joint. They are distinguishable from other bony tumors on x-ray, since they appear to have a nonsclerotic and sharply defined border. Giant cell tumors are typically composed of oval mononuclear cells along with scattered multinucleated giant cells.
Chondrosarcoma more commonly affects the axial skeleton. Ewing sarcoma classically shows onion-skinning on x-ray and primarily affects younger boys. Osteochondromas affect the metaphysis of long bones. Osteosarcoma is more common in younger males and shows periosteal shadowing (Codman triangle) on x-ray.
End Review

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1 ✗
2 ✗
3 ✗
4 ✓
5 ✓
6 ✓
7 ✗
8 ✗

The increased susceptibility to cancer in this family is caused by a mutation in which of the following genes?

- A. *APC*
- B. *BRCA1*
- C. *BRCA2*
- D. *RET*
- ✓ E. p53

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You correctly chose E [66%]

This patient has a history of adrenocortical cancer and now presents with breast cancer based on the pathologic findings of her mass (the image shows high-grade invasive ductal carcinoma with prominent mitotic figures). In addition she has a strong family history (seen in her siblings and her father) of bone, breast, and blood cancers.

This family has **Li-Fraumeni cancer syndrome,** in which one copy of the ***p53*** tumor suppressor gene carries a mutation. This is an autosomal dominant disorder in which family members have a significantly increased risk of malignancy as children or young adults. Typical cancers include osteosarcomas, soft tissue sarcomas, early-onset breast cancers, adrenocortical tumors, and leukemias.

APC, BRCA1, and BRCA2 are all tumor suppressor genes that can result in familial cancer syndromes when one defective copy is passed down between generations. ***RET*** is a proto-oncogene, in which gain of function mutations can result in associated syndromes.

End Review

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2 ✗
3 ✗
4 ✓
5 ✓
6 ✓
7 ✗
8 ✗

- A. Deep femoral artery
- B. Inferior gluteal artery
- ✓ D. Medial femoral circumflex artery
- E. Obturator artery

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6

The correct answer is D [66%]

Fractures of the femoral neck result in increased risk of injury to the **medial femoral circumflex artery**. The medial femoral circumflex artery supplies blood to the femoral head and neck. Therefore tearing of this artery as a result of a femoral neck fracture leads to ischemia of the femoral head. Complications associated with disrupted blood supply to the femoral head via the medial femoral circumflex artery include increased mortality and osteonecrosis of the femoral head.

Femoral fractures usually occur in members of the older population after minor traumas such as falls. There is a higher incidence of fractures in **women** compared with men and in **patients with osteoporosis**. Osteonecrosis rarely occurs in young patients but can occur when the patient has experienced high-impact trauma, such as a direct, blunt force to the leg. Risk factors for osteonecrosis include alcohol abuse, sickle cell disease, trauma, Legg-Calvé-Perthes disease, Gaucher disease, and a slipped capital femoral epiphysis.

Treatment of fractures includes immobilization and pain management with analgesics. Open reduction and internal fixation can be attempted in young patients and patients with displaced fractures. Hip arthroplasty can be performed in older patients.

The other answer choices are incorrect for the following reasons.

- The **lateral femoral circumflex artery** passes anterior to the femoral neck and branches into three arteries. It provides minor blood supply to the femoral head.
- Branches of the **obturator artery** become the artery of ligamentum teres, which provides minor blood supply to the femoral head proximal to the epiphyseal growth plate.
- Disruption of the **deep femoral artery** leads to claudication, not osteonecrosis.
- The **inferior gluteal artery** provides minor contributions of blood supply to the femoral head.

End Review