

MSS

15 USMLE QUESTIONS
(UWORLD + RX)
With clarifications

First 3 lectures of pathology

USMLE-UWORLD Test Bank

Item 4 of 14
Question ID: 987

A 70-year-old man comes to the clinic due to intermittent leg pain and difficulty walking. He describes the pain as mild-to-moderate, deep, and lasting throughout the day. The patient has a history of osteoarthritis in his hands for which he takes over-the-counter nonsteroidal anti-inflammatory drugs, but says that he never has had problems with his knees. Physical examination shows point tenderness over the right tibia. Laboratory studies show elevated serum alkaline phosphatase. Bone biopsy shows haphazardly oriented segments of lamellar bone with prominent cement lines. The initial phase of this patient's disorder involves increased activity of which of the following cell types?

A. Chondrocytes
 B. Endothelial cells
 C. Fibroblasts
 D. Osteoblasts
 E. Osteoclasts

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Answer

Item 4 of 14
Question ID: 987

A 70-year-old man comes to the clinic due to intermittent leg pain and difficulty walking. He describes the pain as mild-to-moderate, deep, and lasting throughout the day. The patient has a history of osteoarthritis in his hands for which he takes over-the-counter nonsteroidal anti-inflammatory drugs, but says that he never has had problems with his knees. Physical examination shows point tenderness over the right tibia. Laboratory studies show elevated serum alkaline phosphatase. Bone biopsy shows haphazardly oriented segments of lamellar bone with prominent cement lines. The initial phase of this patient's disorder involves increased activity of which of the following cell types?

A. Chondrocytes (3%)
 B. Endothelial cells (0%)
 C. Fibroblasts (1%)
 D. Osteoblasts (20%)
 E. Osteoclasts (60%)

Omitted
Correct answer: E
60% Answered correctly
3 Seconds Time spent
09/07/2016 Last updated

Explanation

Paget disease of bone

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TUTOR

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Question ID: 987

Wolke phase (osteoclast + osteoblast)

New bone formation
Osteoblasts

Osteosclerotic phase (osteoblast dominant)

Weak, thickened, woven bone

This elderly patient's bone pain, increased alkaline phosphatase, and biopsy findings are characteristic of **Paget disease of bone (PDB)**, a condition that results in accelerated bone remodeling with eventual bony overgrowth. The disease is thought to be caused by environmental factors and gene mutations (eg, affecting RANK, osteoprotegerin) that result in excessive RANK and NF- κ B activation. This leads to increased osteoclast differentiation and activity. The disease typically progresses through 3 phases:

- 1. Osteolytic (osteoclast-dominant) phase** – characterized by increased numbers of osteoclasts that appear abnormally large with an excessive number of nuclei. Increased resorption activity is prominent.
- 2. Mixed (osteoclast-osteoblastic) phase** – defined by a rapid increase in osteoblastic bone formation with persistent osteoclastic activity.

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3. **Osteosclerotic (osteoblast-dominant) phase** – characterized by continued osteoblastic bone formation and remodeling that result in a dense, hypovascular **mosaic pattern** of lamellar bone with irregular, haphazardly oriented sections separated by **prominent cement lines**. The end result is a thickened, deformed bone that is weaker than normal and prone to fracture.

(Choice A) Chondrocytes are not involved in the pathogenesis of PDB.

(Choices B and C) In the early stages of PDB, the adjacent marrow spaces are replaced by highly vascular stromal tissue as a result of increased endothelial cell and fibroblast proliferation due to cytokines secreted by osteoclasts. The increased vascularity causes arteriovenous shunting that can result in high-output heart failure.

(Choice D) Although this patient's bone biopsy shows findings characteristic of the osteosclerotic (osteoblast-dominant) phase of Paget disease, the question is specifically asking about the **initial (osteolytic) phase** of Paget disease, where osteoclast activity is predominantly increased. Increased activity and dysregulation of osteoblasts and fibroblasts increase the risk of developing sarcomas (eg, osteosarcoma) in patients with PDB.

Educational objective:
Bone pain and elevated alkaline phosphatase level in an elderly patient can occur with osteoblast metastases and Paget disease of bone (PDB). Biopsy showing a mosaic pattern of lamellar bone is diagnostic for PDB. The initial phase in PDB is characterized by an increase in osteoclastic activity.

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Paget disease of bone

Osteolytic phase (osteoclast dominant)

Osteoclasts

Mixed phase (osteoclast + osteoblast)

New bone formation
Osteoblasts

Osteosclerotic phase (osteoblast dominant)

Weak, thickened, woven bone

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Exhibit Display

Osteoclast differentiation

Stromal cell

M-CSF

Osteoblast

Osteoclast precursor

RANK

Deferoxamine

Fusion

Resorptive pit

High OPN/RANK L cells

Low OPN/RANK L cells

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TUTOR

Item 6 of 14
Question ID: 640

Tutorial Lab Values Notes Calculator Reverse Color Text Zoom

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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2/12/2019

Answer

Item 6 of 14
Question ID: 640

Tutorial Lab Values Notes Calculator Reverse Color Text Zoom

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 [4%]
- B. Decreased osteocyte apoptosis [3%]
- C. Decreased osteoid formation [2%]
- D. Increased bone resorption [87%]
- E. Increased osteoprotegerin levels [2%]

Correct answer: D

77% Answered correctly 3 Seconds Time Spent 08/21/2018 Last Updated

Explanation

Hematopoietic stem cell

Osteoclast differentiation

Block Time Remaining: 00:00:28
TUTOR

Item 6 of 14
Question ID: 640

Tutorial Lab Values Notes Calculator Reverse Color Text Zoom

Osteoclast differentiation

The diagram illustrates the process of osteoclast differentiation. It starts with a Hematopoietic stem cell that differentiates into an Osteoclast precursor under the influence of M-CSF. The Osteoclast precursor expresses RANK. Simultaneously, Bone marrow stromal cells differentiate into Osteoblasts and Osteocytes, with the Osteoblasts expressing RANK-L. The interaction between RANK on the precursor and RANK-L on the stromal cells leads to Fusion, Activation, and Survival, resulting in a Multinuclear osteoclast. Additionally, Osteoblasts express Osteoprotegerin, which competitively binds to RANK-L, preventing it from binding to RANK on the precursor.

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The diagram illustrates the RANK/RANKL/OPG signaling pathway. On the left, a macrophage (MΦ) produces RANKL, which binds to RANK on an osteoblast. This interaction leads to "Fusion, Activation, Survival" of osteoclasts, resulting in a "Multinuclear osteoclast". Below this, a box states: "Low OPG/RANKL ratio: increased osteoclast formation & activity". On the right, "Osteoprotegerin" is shown as a decoy receptor that "competitively binds RANKL & prevents its binding to RANK". Below this, a box states: "High OPG/RANKL ratio: decreased osteoclast formation & survival".

The 2 most important factors in osteoclast differentiation are macrophage colony-stimulating factor (M-CSF) and receptor activator of nuclear factor kappa B ligand (RANKL), which stimulate the development of mature, multinucleated osteoclasts. The interaction of RANKL with RANK (receptor) is blocked by osteoprotegerin (OPG), which acts as a decoy receptor. By binding RANKL, 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 RANKL; bone turnover increases when OPG is low and RANKL 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

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Item 11 of 14
Question ID: 700

Tutorial Lab Values Notes Calculator Reverse Color Text Zoom

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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Answer

Item 11 of 14
Question ID: 700

Tutorial Lab Values Notes Calculator Reverse Color Text Zoom

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 [89%]
 B. Hypothalamic neurosecretory cells [2%]
 C. Osteoblasts [3%]
 D. Osteoclasts [1%]
 E. Pituitary somatotrophs [8%]

Correct answer: A
86% Answered correctly
3 Seconds Time Spent
09/11/2018 Last Updated

Explanation

Achondroplasia features

Block Time Remaining: 00:00:41
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Question ID: 700

Tutorial Lab Values Notes Calculator Reverse Color Text Zoom

Correct answer: A
86% Answered correctly
3 Seconds Time Spent
09/11/2018 Last Updated

Explanation

Achondroplasia features

Block Time Remaining: 00:00:41
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Item 11 of 14
Question ID: 700

Tutorial Lab Values Notes Calculator Reverse Color Text Zoom

Macrocephaly

Block Time Remaining: 00:00:41
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Item 11 of 14
Question ID: 700

Tutorial Lab Values Notes Calculator Reverse Color Text Zoom

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This patient's limb shortening with normal torso length, specific craniofacial features (frontal bossing, midface hypoplasia), and risk of passing the condition to her offspring (50%) are characteristic of **achondroplasia**. The condition is caused by an **autosomal dominant** point mutation in the fibroblast growth factor receptor 3 (FGFR3) gene; 90% are de novo (unaffected parents) and 10% are inherited. Because the mutation is **autosomal dominant**, the fetus of an affected and an unaffected parent has a 50% chance of inheriting the mutation.

Achondroplasia affects **endochondral ossification**, the process that makes **long bones** (eg, humerus, femur, phalanges) and portions of the skull and face. In endochondral bone formation, mesenchymal cells differentiate into chondrocytes that secrete cartilage matrix. These chondrocytes continue to proliferate through childhood, forming an elongating cartilage template that progressively becomes calcified and later invaded by osteoblasts, osteoclasts, and blood vessels originating from the periosteum. Deposition of osteoid matrix over the septa of calcified cartilage matrix forms woven bone, which then undergoes remodeling into compact bone.

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Item 11 of 14
Question ID: 700

Tutorial Lab Values Notes Calculator Reverse Color Text Zoom

autosomal dominant, the fetus of an affected and an unaffected parent has a 50% chance of inheriting the mutation.

Achondroplasia affects **endochondral ossification**, the process that makes **long bones** (eg, humerus, femur, phalanges) and portions of the skull and face. In endochondral bone formation, mesenchymal cells differentiate into chondrocytes that secrete cartilage matrix. These chondrocytes continue to proliferate through childhood, forming an elongating cartilage template that progressively becomes calcified and later invaded by osteoblasts, osteoclasts, and blood vessels originating from the periosteum. Deposition of osteoid matrix over the septa of calcified cartilage matrix forms woven bone, which then undergoes remodeling into compact bone.

FGFR3 is normally responsible for limiting chondrocyte proliferation during endochondral ossification. In achondroplasia, FGFR3 becomes constitutively activated, causing exaggerated **inhibition of chondrocyte proliferation** that results in the characteristic bone shortening and craniofacial abnormalities.

(Choices B and E) Hypothalamic or pituitary results (eg, tumor, ischemia) can result in defective release of either hormone. GH deficiency can lead to proportional short stature (both long and fat bones affected) as opposed to the disproportionate short stature seen in achondroplasia (only long bones affected).

(Choice C) The flat bones (eg, most of the skull, pelvis) form primarily via **intramembranous (not endochondral) ossification**. In intramembranous ossification, mesenchymal cells differentiate directly into osteoblasts and begin osteoid matrix secretion without the formation of cartilaginous bones. As a result, most flat bones remain unaffected in achondroplasia.

(Choice D) Osteoclasts are specialized macrophages that function to resorb bone. **Paget disease**, characterized by disordered bone mass, initially begins with excessive activity of abnormally large osteoclasts followed by osteoblastic activity and eventual sclerosis. Patients are usually elderly and can present with focal bone pain and pathologic fractures.

Educational objective: Unlike the process of intramembranous ossification that forms flat bones, endochondral ossification proceeds along a cartilage template and is responsible for the formation of long bones. Achondroplasia is characterized by an exaggerated inhibition of chondrocyte proliferation in the growth plates of long bones and manifests with proximal limb shortening, midface hypoplasia, and macrocephaly.


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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.



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 Mark Previous Next Lab Values Notes Calculator Reverse Color Text Zoom

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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

Suspend End Block

A 62-year-old white woman comes to her family doctor because of lower back pain located over the spine. When asked about the onset of 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 past 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

S
Suspend End B

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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

S
Suspend End B

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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

5

Suspend End Block

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Item: 7 of 13
QID: 39382.2

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A 65-year-old man comes to the clinic because of a persistent headache, dizziness, and severe hip pain during the past year. He says that his hat no longer fits him. He also reports ringing in his ear and some hearing loss. He has a history of hypertension and diabetes mellitus controlled with lisinopril and metformin. His paternal grandfather had osteosarcoma. Temperature is 37.5°C (99.6°F), blood pressure is 126/82 mm Hg, pulse is 79/min, and respiratory rate is 16/min. Physical examination elicits bone pain. Serum calcium, parathyroid hormone, and phosphorus levels are within reference ranges.

Elevation of which of the following markers is associated with this patient's most likely cause of bone pain?

A. Alkaline phosphatase
 B. Calcitonin
 C. Gamma-glutamyl transferase
 D. Tartrate resistant acid phosphatase
 E. Urinary deoxypyridinoline

6

Suspend End Block

Item: 8 of 13
QID: 5092.4

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A mother brings her 2-month-old daughter to the emergency department because of lethargy and a fever of 39.2°C (102.6°F). The mother is also concerned because the infant is not gaining weight.

Physical examination reveals that the infant has an increased head circumference and prominent hepatosplenomegaly. Mastoid and paranasal sinus malformations are also noted during the course of the workup. Results of laboratory tests are as follows:

HGB: 7.9 g/dL,
Hct: 28%,
WBC: 373/μL,
MCV: 78.2
Reticulocyte count: 6.5%

Despite fluid resuscitation and initiation of antibiotic therapy, the infant dies. On autopsy, histologic analysis of the bone marrow reveals a lack of a medullary canal, with persistence of the primary spongiosa, and deposition of dense, sclerotic bone.

Which malfunctioning cells are the cause of this patient's disease process?

A. Lymphoid progenitor cells
 B. Osteoblasts
 C. Osteoclasts
 D. Osteocytes
 E. Reticulocytes

7

Item: 9 of 13
QID: 4763.12

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A 9-month-old girl who was born at full term is brought by her mother to the pediatrician for evaluation of abnormal stature and growth. The mother comments that she has noticed her child's stature being "different from her peers ever since birth." Both labor and pregnancy were uncomplicated. The patient has remained below the third percentile for height in all of her pediatric visits to date. The mother is above-average height; however, the father's height is slightly below-average and they wonder if she will eventually "outgrow" this phase. The patient has no other medical conditions and is up to date with vaccinations. On examination, the child has short stature with rhizomelic limb shortening and a prominent forehead. She appears to be on pace with cognitive milestones, babbling during the visit and laughing when the mother plays peek-a-boo with her. Her examination is otherwise unremarkable.

An abnormality in which of the following is the most likely cause of this patient's condition?

A. Bone resorption
 B. Collagen formation
 C. Endochondral ossification
 D. Membranous ossification
 E. Mucopolysaccharide degradation

8

Suspend End Block

Item: 10 of 13
QID: 1664.21

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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

9

Suspend End Block

Item: 13 of 13
QID: 2610.14

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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

10

Suspend End Block

Item: 12 of 13
QID: 4446.20

Mark Previous Next Lab Values Notes Calculator Reverse Color Text Zoom

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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

Suspend End Block

Answers

Item: 1 of 13
QID: 5093.5

1 ✓
2 ✓
3 ✗
4 ✓
5 ✓
6 ✓
7 ✓
8 ✓
9 ✓
10 ✓
11 ✓
12 ✓
13 ✓

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

3 ✗
4 ✓
5 ✓
6 ✓
7 ✓
8 ✓
9 ✓
10 ✓
11 ✓
12 ✓
13 ✓

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

3 ✗
4 ✓
5 ✓
6 ✓
7 ✓
8 ✓
9 ✓
10 ✓
11 ✓
12 ✓
13 ✓

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 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

Item: 6 of 13
QID: 3920.15

Mark Previous Next

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

3

We Value Your Feedback!

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**,

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

Item: 5 of 13
QID: 39423.2

Mark Previous Next Lab Values Notes Calculator Reverse Color Text Zoom

3 X
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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

4

We Value Your Feedback!

You correctly chose C [69%]

This young child presenting with widening and thickening of the wrist bones, craniotabes, and genu varum ("bowed legs") is suffering from **rickets**. His diet and dark skin predispose him to **vitamin D deficiency** and consequent **impairment of bone mineralization**, which is likely causing his condition.

Item: 4 of 13
QID: 3806.13

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

We Value Your Feedback!

5

You correctly chose B [66%]

This patient who initially presents with shortness of breath and back pain is found to be suffering from **osteoporosis**, which is characterized by low bone mass and increased bone fragility, leading to an increased risk of fractures. Her diagnosis is confirmed by the findings seen in the DEXA scan below, which reveals a vertebral fracture and loss of bone density.

Clinically, osteoporosis is defined by a bone mineral density T-score ≥ 2.5 standard deviations below the mean of the ideal population, with values between 1 and 2.5 standard deviations defined as osteopenia. Risk factors include:

- female gender
- advanced age
- a previous fracture
- low body weight

End Review

Item: 4 of 13
QID: 3806.13

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characterized by low bone mass and increased bone fragility, leading to an increased risk of fractures. Her diagnosis is confirmed by the findings seen in the DEXA scan below, which reveals a vertebral fracture and loss of bone density.

Clinically, osteoporosis is defined by a bone mineral density T-score ≥ 2.5 standard deviations below the mean of the ideal population, with values between 1 and 2.5 standard deviations defined as osteopenia. Risk factors include:

- female gender
- advanced age
- a previous fracture
- low body weight
- smoking, and
- excess alcohol intake

Following initiation of treatment for her osteoporosis, the patient presents at the emergency department with dysphagia and burning chest pain, evidence of a **bleeding ulcer** that can originate from either the stomach or esophagus. This is most likely an **erosive lesion, which is a possible adverse effect of bisphosphonate therapy** (with drugs such as **alendronate**) for osteoporosis.

In order to avoid this potentially serious complication, patients are advised to stay upright for at least half an hour after taking bisphosphonates to ensure rapid transit through the stomach. Optimal duration of alendronate use has not been determined. For patients at low risk for fracture, consider drug discontinuation after 3-5 years of use. Other medications that can cause esophagitis include antibiotics (clindamycin, tetracycline, and doxycycline), potassium chloride, quinidine, aspirin and anti-inflammatory agents. Oral bisphosphonates have also been associated with an increased risk of jaw necrosis.

Vitamin D, denosumab, and estradiol can be used to treat osteoporosis but do not cause esophagitis. **Ibuprofen** can cause esophagitis but is not used to treat osteoporosis. **Tamoxifen** is not used to treat osteoporosis and does not cause esophagitis.

End Review

3 X
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A. Alkaline phosphatase
 B. Calcitonin
 C. Gamma-glutamyl transferase
 D. Tartrate resistant acid phosphatase
 E. Urinary deoxypyridinoline

We Value Your Feedback!

6

You correctly chose A [85%]

This patient is a 65-year-old man with a history of hypertension and diabetes mellitus who has severe **bone pain, headache, tinnitus, vertigo, and hearing loss**. This is most suggestive of **Paget disease**.

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).

3 X
4 ✓
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Which malfunctioning cells are the cause of this patient's disease process?

A. Lymphoid progenitor cells
 B. Osteoblasts
 C. Osteoclasts
 D. Osteocytes
 E. Reticulocytes

We Value Your Feedback!

7

You correctly chose C [53%]

This patient with severe anemia and leukopenia, prominent hepatosplenomegaly, and bony malformations in the skull and long bones most likely had **osteopetrosis**. This rare hereditary disorder results from a failure of the resorption and remodeling of bone due to malfunctioning **osteoclasts**. The skeleton becomes diffusely sclerotic and dense as new bony matrix is laid into the medullary canal, replacing the hematopoietic tissue. Calcified remnants of the primary spongiosa, which is normally removed during growth, are seen within the mature bone. Compensation is achieved by **extramedullary hematopoiesis**, leading to **hepatosplenomegaly**. Despite the increased density, the bone is brittle and predisposed to fracture.

There are two main types of osteopetrosis, each one characterized by inheritance pattern. The autosomal-recessive form is more aggressive and is often fatal in utero or in the neonatal period. The autosomal dominant form is usually benign and may be discovered incidentally on x-ray films.

End Review

Item: 9 of 13
QID: 4763.12

Mark Previous Next Lab Values Notes Calculator Reverse Color Text Zoom

3 X
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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 in life, which are not present in this patient's history.

End Review

Item: 10 of 13
QID: 1664.21

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3 X
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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

Item: 11 of 13
QID: 4865.11

Mark Previous Next Lab Values Notes Calculator Reverse Color Text Zoom

3 X
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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

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
- B. Ewing sarcoma
- C. Metastatic adenocarcinoma
- D. Osteoid osteoma
- E. Osteosarcoma

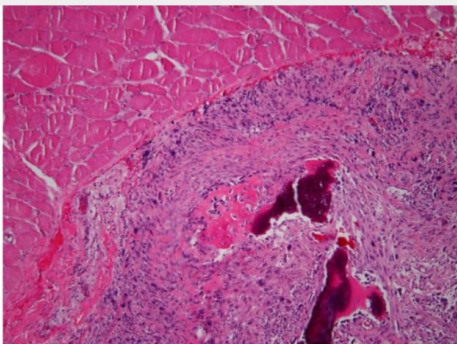
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1

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Item 28 of 28
Question ID: 15636

Exhibit Display



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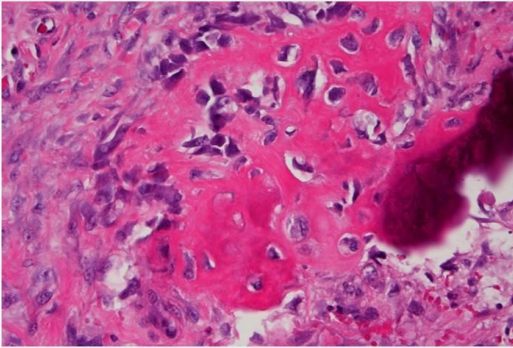
Item 28 of 28
Question Id: 15636

Mark Previous Next

Tutorial Lab Values Notes Calculator Reverse Color Text Zoom

Exhibit Display

Exhibit 1 Exhibit 2



Zoom In Zoom Out Reset Add To Flash Card

Block Time Remaining: 00:03:11
TUTOR

Feedback Suspend End Block

10:12 PM
2/12/2019

Item 15 of 28
Question Id: 721

Mark Previous Next

Tutorial Lab Values Notes Calculator Reverse Color Text Zoom

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

Submit

2

Block Time Remaining: 00:01:15
TUTOR

Feedback Suspend End Block

10:06 PM
2/12/2019

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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

3

- 1
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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

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.

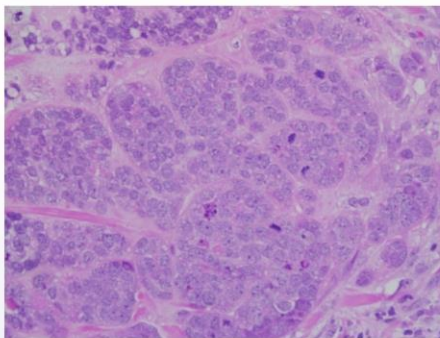


Image courtesy of Difu Wu

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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8

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

6

 Suspend

 End Block

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 [9%]
- E. Osteosarcoma [55%]

Omitted
Correct answer: E
55% Answered correctly
27 Seconds Time Spent
02/04/2019 Last Updated

Explanation



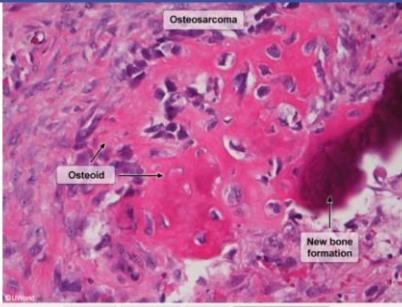
Border of osteosarcoma

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1

Item 28 of 28
Question ID: 15636

Exhibit Display



Osteosarcoma

Osteoid

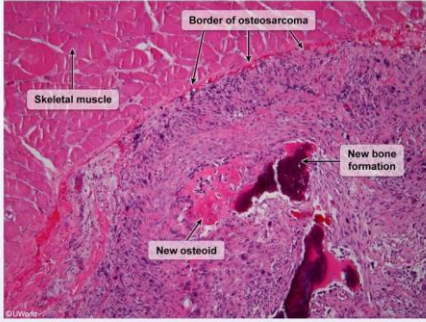
New bone formation

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Block Time Remaining: 00:03:19
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Item 28 of 28
Question ID: 15636

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

Block Time Remaining: 00:03:19
TUTOR

Item 28 of 28
Question ID: 15636

Explanation

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.

Block Time Remaining: 00:03:19
TUTOR

Item 15 of 28
Question ID: 721

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%]

Omitted
Correct answer: D
39% Answered correctly
4 Seconds Time Spent
01/05/2019 Last Updated

Explanation

Progression of hematogenous osteomyelitis

Block Time Remaining: 00:01:17
TUTOR

Item 15 of 28
Question ID: 721

bacterial seeding results in focal bone marrow cellulitis

inflammation within confined space compromises blood flow, causing necrosis

infection forces through vascular channels into the cortex and spreads along periosteum

©UWorld

Development of chronic sequelae

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 epiphyseal closure.

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

Block Time Remaining: 00:01:17
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Item 15 of 28
Question ID: 721

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 epiphyseal closure.

Hematogenous osteomyelitis begins with a seeding event that causes an acute cellulitis of the bone marrow. The resulting inflammation within the confined bony 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 fenestrations in this region. Without proper treatment, the infection can progress to chronic suppurative osteomyelitis.

Block Time Remaining: 00:01:17
TUTOR

Item: 3 of 8
QID: 5010.12

1 X
2 X
3 X
4 ✓
5 ✓
6 ✓
7 X
8 X

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

We Value Your Feedback

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

Item: 3 of 8
QID: 5010.12

1 X
2 X
3 X
4 ✓
5 ✓
6 ✓
7 X
8 X

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

Item: 4 of 8
QID: 3381.12

1 X
2 X
3 X
4 ✓
5 ✓
6 ✓
7 X
8 X

B. Ewing sarcoma
 C. Giant cell tumor
 D. Osteochondroma
 E. Osteosarcoma

We Value Your Feedback

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

Item: 6 of 8
QID: 1261.14



Mark Previous Next Lab Values Notes Calculator Reverse Color Text Zoom

1 X
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3 X
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5 ✓
6 ✓
7 X
8 X

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

We Value Your Feedback!

  5

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



Item: 7 of 8
QID: 39378.3

Mark Previous Next Lab Values Notes Calculator Reverse Color Text Zoom

1 X
2 X
3 X
4 ✓
5 ✓
6 ✓
7 X
8 X

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

We Value Your Feedback!

  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