

1. What best characterizes NORMAL synovial fluid?
  - A) Contains polysaccharide to lubricate the cartilage
  - B) Contains protein to lubricate the articular cartilage
  - C) Glucose  $\approx$  66% of serum glucose
  - D) Opaque fluid
  - E) Rarely contains  $< 5$  WBC/cc
  - F) All of the above are true
  
2. What is articular collagen composed of?
  - A) Type I collagen, proteoglycan, fenestrated capillaries
  - B) Type II collagen, proteoglycan, chondrocytes
  - C) Type III collagen, proteoglycan, acellular
  - D) Type IV collagen, Type A (macrophage-like) and B (fibroblast-like) cells
  
3. Where are the receptors for calcitonin and PTH found, respectively?
  - A) Calcitonin: Osteoblast; PTH: Osteoblast
  - B) Calcitonin: Osteoblast; PTH: Osteoclast
  - C) Calcitonin: Osteoclast; PTH: Osteoblast
  - D) Calcitonin: Osteoclast; PTH: Osteoclast
  
4. A defect in CBFA1 would cause
  - A) Abnormal expression of HOX genes
  - B) Decreased bone resorption
  - C) Empty Howship's lacunae
  - D) Normal skeleton morphology, but composed entirely of collagen
  - E) Syndactyly
  
5. What is a downstream event in the signaling pathway of PTH?
  - A) Decreased gene expression of NF $\kappa$ B
  - B) Increased gene expression of osteoprotegerin
  - C) Increased proliferation of osteoclasts
  - D) Increased vitamin D1 synthesis
  - E) Upregulation of Receptor Activator of NF $\kappa$ B Ligand
  
6. What bone is not formed from a cartilage "template"?
  - A) First rib
  - B) Hyoid Bone
  - C) Maxilla
  - D) Sphenoid bone
  - E) Tibia

7. What defect is NOT caused by a mutation in a HOX gene?
- A) Abnormal closure of skull
  - B) Dwarfism
  - C) Supernumerary digits
  - D) Supernumerary ribs
  - E) Syndactyly (fused digits)
8. What statement INCORRECTLY matches a type of bone with its characteristic?
- A) Cortical bone: composed of circumferential, concentric, and interstitial bone, which are all subtypes of lamellar bone
  - B) Lamellar bone: layers of bone matrix that are stronger than woven bone
  - C) Osteoid: unmineralized bone matrix
  - D) Trabecular bone: a subtype of lamellar bone found in the medullary cavity
  - E) Woven bone: highly ordered Type I collagen weave that is normal in the fetus
9. An child has many fractures, lacks energy, and has a history of infections. A CBC shows significant anemia and neutropenia. What is the single MOST LIKELY cause of these symptoms?
- A) Defect in carbonic anhydrase II
  - B) Decreased growth hormone
  - C) Defect in Type I collagen
  - D) Defect in Type IV collagen
  - E) Defect in Vitamin D metabolism
  - F) Hyperparathyroidism
10. A 59 year old woman falls and breaks her hip. A DEXA scan reveals significantly decreased bone density, and she is started on supplemental vitamin D and bisphosphonates. What is the best way to check the effects of therapy?
- A) Serum alkaline phosphatase
  - B) Serum  $\text{Ca}^{2+}$
  - C) Urine  $\text{Ca}^{2+}$
  - D) Urine hydroxyproline
  - E) Urine N-telopeptide (NTX)
11. Two of your patients have vitamin D abnormalities. One has rickets and the other has osteomalacia. What is the significantly difference between these two patients?
- A) Age
  - B) Diet
  - C) Race
  - D) Serum  $\text{Ca}^{2+}$
  - E) Underlying pathogenesis
12. A 58 year old man has a cystic, hemorrhagic lesion in his mandible. His labs are notable for a creatinine of 8. He also has abnormal hands. What else would you expect to see?
- A) Evidence of an osteosarcoma
  - B) Gouty tophi around his ear
  - C) High output cardiac failure
  - D) Osteonecrosis of the scaphoid bone in the wrist
  - E) Subperiosteal resorption of the phalanx and distal tuft on hand X-Ray

13. An elderly man complains of tiredness. You notice that even though his clothes are pretty well-worn, he has a brand new hat. When you ask him about the hat, he says that he just got it because his old hat “just seemed really snug.” A workup reveals anemia. What would you be MOST LIKELY to also find?
- A) Decreased alkaline phosphatase
  - B) Evidence of decreased osteoblastic activity
  - C) Evidence of decreased osteoclastic activity
  - D) Increased growth hormone
  - E) Low-output cardiac failure
  - F) Paresthesias
14. What is NOT a complication of chronic osteomyelitis?
- A) Amyloid
  - B) Endocarditis
  - C) Sarcoid
  - D) Sarcoma of infected bone
  - E) Squamous cell carcinoma of infected fistula tract
15. A 45 year old woman has morning stiffness and both of her hands are tilted towards the ulnar side of her wrist. What is the pathogenesis of this disease?
- A) Activated synovial cells
  - B) Drug reaction
  - C) HLA-B27 molecular mimicry
  - D) Inappropriately activated CD8+ cells
  - E) Increased uric acid
  - F) Mechanical wear and tear on the articular cartilage
16. The patient in #15 has nodules on her hands. After biopsy, how would it look microscopically?
- A) Blue-black pigment prominent
  - B) Fibrocartilage “flowing” over articular cartilage
  - C) Necrosis with palisading macrophages
  - D) Negatively birefringent crystals
  - E) Positively birefringent crystals
17. Who would be most likely to have bamboo spine?
- A) A panda
  - B) Someone who is HLA-B27
  - C) Someone who is HLA-DR2/DR3
  - D) Someone who is HLA-DR4
  - E) Someone with severe scoliosis

19-22: Mix and Match the joints

- A) CMC (base of thumb)
- B) MCP
- C) PIP
- D) DIP

18. Heberden node

19. Bouchard node

20. Osteoarthritis (three answers)

21. Rheumatoid arthritis (two answers)

22. What drug is NOT known to cause drug-induced lupus?

- A) Chlorpromazine
- B) Hydralazine
- C) Isoniazid
- D) Methyldopa
- E) Procainamide
- F) Skittles

23. A 32 year old woman has a malar “butterfly” rash. What other organ system is MOST likely to be involved?

- A) CNS
- B) Joints
- C) Kidney
- D) Mucous membrane
- E) Pericardium

24. A 38 year old woman’s face looks like it is pulled too tight. She also has stiff fingers and restrictive lung disease. What is the instigating event, and what antibody would you expect to find?

- A) Instigating event: Hyperactive B cells; Antibody: anti-Scl-70
- B) Instigating event: Hyperactive B cells; Antibody: anti-Sm
- C) Instigating event: vascular injury; Antibody: anti-Scl-70
- D) Instigating event: vascular injury; Antibody: anti-Sm

## Answers:

1. **A.** Normal synovial fluid contains hyaluronan, which is a high molecular-weight polysaccharide that lubricates the articular cartilage. The fluid is clear, has serum glucose, and can contain up to 200 WBC/cc.
2. **B.** Articular cartilage is composed of Type II collagen for tensile strength. The hydrophilic glycosaminoglycans absorb and release water in response to compression, with a functional effect like a very stiff spring. About 1-2% of the volume of the cartilage is composed of chondrocytes, so it is relatively hypocellular. Cartilage is avascular, it is nourished entirely by diffusion of nutrients from the synovial fluid. Choices (A) and (C) are nonsense. Even though (D) is similar to the synovial lining (which makes synovial fluid), synovial lining does NOT have a basement membrane.
3. **C.** It's important to remember that the only hormone receptor on the osteoclast is the receptor for calcitonin. The PTH, vitamin D, and estrogen receptors are on the osteoblast.
4. **D.** Knockout mice lacking CBFA1 gene have nonfunctional osteoblasts and failed mineralization of bone, even though the patterning of the skeleton is normal. Osteoclasts live in howship's lacunae, and osteoclasts are unaffected.
5. **E.** PTH causes an increased in RANKL on osteoblasts, as does vitamin D3, IL-11, and some malignancies (causing hypercalcemia of cancer). Osteoprotegerin opposes the effect of RANKL by acting as a decoy receptor. On osteoclasts, RANKL acts to stimulate osteoclast *differentiation*, as contrasted with M-CSF's ability to increase osteoclast *proliferation*. PTH causes increased D3 synthesis in the kidney, but the synthesis of vitamin D1 is dependent on sunlight and is independent of PTH.
6. **C.** Ok, picky question, I admit, but I think it's important for boards if not for this test. Bones formed by *Endochondral ossification* are formed from a cartilage template (just remember the "chondral" in the name). All bones south of the head (and a few skull bones) are formed this way. Bones formed by *Intramembranous ossification* are formed directly from an ossification center that forms in embryonic mesoderm. Most bones of the skull are formed intramembranously except the ethmoid, sphenoid, petrous part of the temporal bone, and some random bones of the ear.
7. **B.** HOX genes are responsible for the body layout. Dwarfism is caused by a mutation in the cell-signalling protein FGR3. The two main types of dwarfism are Achondroplasia (AD inheritance, normal lifespan, propensity to wear red hats and smoke gnarled pipes) and Thanatrophic dwarfism (early death from respiratory collapse).
8. **E.** Woven bone has a *disordered* structure. It is true, however, that it is normal in the fetus. Woven bone is pathological in the adult, but can be found in fractures, osteomyelitis, or bone-forming tumors. There are four types of lamellar bone: circumferential, concentric, and interstitial (all three found in the cortex) and trabecular (found in the medullary cavity).

9. **A.** The child has osteopetrosis (marble bone disease). The root of the disease is an inability to resorb bone caused by a lack of carbonic anhydrase II → no HCl can be formed → no bone resorption. Clinically, the disease presents with fractures, and anemia and cytopenias due to lack of marrow space. Defects in type I collagen cause osteogenesis imperfecta, but wouldn't explain the cytopenia and anemia. A child with a vitamin D deficiency would result in rickets (bowed legs). Hyperparathyroidism can also lead to fractures, but is typically seen in renal failure or older patients, and wouldn't explain the cytopenia or anemia.
10. **E.** Measuring the N-telopeptide is the most useful way to track the progress of therapy and compliance in osteoporosis. Alkaline phosphatase is released by osteoblasts and is significantly increased in blastic lesions of bone, such as prostate metastasis (but NOT in multiple myeloma, which typically forms lytic lesions). Increased urinary hydroxyproline is a good test for Paget's disease. The serum  $\text{Ca}^{2+}$  in patients with osteoporosis should be normal.
11. **A.** Vitamin D deficiency in kids is called Rickets, and vitamin D deficiency in adults is called osteomalacia.
12. **E.** He has hyperparathyroidism, probably secondary to renal failure. The hand lesion is absolutely pathognomonic for hyperparathyroidism. The jaw lesion is *Osteitis fibrosa cystica* and is caused by cytokines released by hyper-activated osteoclasts. If he had had many such cystic brown "tumors" then he would have von Recklinghausen's disease of bone (not to be confused with neurofibromatosis I, which is also called von Recklinghausen's disease, and is associated with café au-lait spots and neurofibromas). In renal failure, calcium is low due to decreased renal activation of vitamin D, which causes PTH levels to rise in a spiral. Osteosarcoma and high-output cardiac failure can sometimes arise from Paget's disease.
13. **F.** He has Paget's disease of bone. This is a disease of hyperstimulated osteoclasts. It probably has a viral etiology, which increases M-CSF and IL-6. Osteoblasts are also stimulated, but not to the extent that osteoclasts are. Two key complications of Paget's are nerve compressions due to paresthesias, and high (not low!) output cardiac failure due to arterio-venous fistulas formed in bone. Rarely, an osteosarcoma can develop. Serum alkaline phosphatase is ↑ due to the osteoblasts. When someone's hat doesn't fit anymore, immediately think of Paget's or an increase in growth hormone. In this case, the GH wouldn't explain the anemia, so Paget's is a better diagnosis. Also, this is not the endocrine block of BOD.
14. **C.** No one knows what causes Sarcoid, but some people think it's pine trees. Any chronic inflammatory process can cause amyloid due to β-pleated sheet formation of acute-phase proteins. Cancers can also arise out of chronically inflamed tissues.
15. **A.** She has rheumatoid arthritis, which is caused by out-of-control synovial cells. T cells probably inappropriately activate these cells, causing a release of proteinases (joint destruction) and cytokines (propagation). Choice (E) describes osteoarthritis.
16. **C.** It's probably worth memorizing each of these lines, because I'm willing to bet that at least one of them will be on the test. The nodules that she has are rheumatoid nodules, which are described in (C). Choice (A) describes what you would find in joints in alkaptonuria (ochronosis), which is due to a deficiency of homogentisic oxidase, causing the blue-black pigment homogentisic acid to accumulate. You wanna know what's cool? Homogentisic acid is made from Tyrosine. What else is made from Tyrosine that's pigmented? Melanin! Now we'll never forget that. Let's also not forget that epinephrine, dopamine, and thyroid hormone are all based on tyrosine. Pretty cool little bugger. (B) describes an osteophyte from osteoarthritis. (D) describes the monosodium urate crystals in gout. (E) describes the calcium pyrophosphate dihydrate crystals in pseudogout (In Pseudogout, CPPD crystals are **P**ositively birefringent and **P**urple).

17. **B.** Bamboo spine is the end result of ankylosing spondylitis, which is associated with HLA-B27 90% of the time. It's kind of a stupid question, because MOST people with HLA-B27 don't have a seronegative spondyloarthropathy. HLA-DR4 is associated with RA, and HLA-DR2/DR3 is associated with lupus.
18. **D.**
19. **C.**
20. **A, C, D.**
21. **B, C.**
22. **F.**
23. **B.** In SLE, joints are involved in 90%. Skin rashes are found in 70% of patients, pericardium 60%, and kidney 50%. CNS and mucous membranes are only found in about 15%.
24. **C.** She has systemic sclerosis. Anti-Scl-70 antibodies is the most specific. The primary lesion is believed to be endothelial cell injury, which causes a cascade of cytokine release and eventual systemic fibrosis. Choice (B) describes lupus.