Harvard-MIT Division of Health Sciences and Technology HST.021: Musculoskeletal Pathophysiology, IAP 2006

Course Director: Dr. Dwight R. Robinson

Final Exam Answers HST.021/HST.020 IAP 2006

1. Wolff's law is that the structure (of bones) adapts to the stresses that the bone experiences.

One example is the development of the tibia, which starts out round, and due to weight and muscle stresses becomes triangular.

Another example is fractures. If the bone is not allowed to feel the stresses, the fracture will not heal, and similarly, the healing process is governed by stresses.

Finally, when people initiate a heavy exercise regime, their bones increase in size to adapt to the new stresses.

- 2. a. Woven bone is characterized by disorganized Type I collagen with many osteocytes of various sizes and shapes. Produced with rapid deposition. Woven is more pleomorphic. Lamellar is characterized by Collagen I in a parallel arrangement and few osteocytes, which are similar in size. Deposition is slow.
- b. Woven and lamellar bone serve different purposes throughout life. Woven bone in an adult is abnormal and signifies pathology including fracture, tumor, etc. Newborns have purely woven bone, and as such, their skeletons are not as strong. The relative quantities of lamellar and woven bone are informative as to the phase of growth for children. Therefore, this can be used as an index to ensure proper development.
- 3. See problem set.
- a. Osteoblasts come from osteoprogenitor cells from mesenchymal stem cells, while osteoclasts come from the macrophage lineage (hematopoeitic).
- b. Osteoblasts lay down mineralized bone, while osteoclasts resorb mineralized bone and cartilage.
- c. Osteoblasts are stimulated by growth factors, cytokines, and estrogen. PTH induces osteoblasts to activate osteoclasts, which occurs through IL-1, IL-6, IL-3, IL-11, and other cytokines and growth factors. Osteoclasts are also responsive to calcitonin.
- d. Osteoblasts are high in mitochondria, ER, golgi, and ribosomes for secretion. The hydroxyappeatite compound is actually stored in the mitochondria. Osteoclasts have high quantities of lysosomes and have a brush border on the side adjacent to the bone. The are multinucleated.
- e. Osteoblasts do not function properly in osteoporosis type II. Osteoclasts do not function properly in osteopetrosis.
- 4. Nutrient artery passes through the cortex to the marrow and subsequently reperforates, serving the inner 1/3 of the cortex (the endosteum). Perforant arteries are from the overlying musculature and serve the outer 2/3 of cortex. Within the bone, blood passes through Haversian system, via the Haversian canals (parallel to the bone axis) and the Volmann's canals (perpendicular to the bone axis).

- 5. The epiphysis is the area of bone beyond the growth plate that typically undergoes hemispherization. It is the end of the bone. The metaphysic is the region between the physis and the end of trabecular bone. The diaphysis is the shaft it is the area of cortical bone with a marrow center. The primary center of ossification is the initial site of vascularization, where bone growth is initiated. Primary trabecula/spongiosum is when the cartilage anlage has started to get replaced with bone. Sections are composed of cartilage surrounded by bone, which are known as primary spongiosum.
- 6. Reiter's syndromy, Lyme disease.

Correct are listed:

- 7. Proteoglycan, superficial, minor, other mechanisms, growths.
- 8. monosodium urate

a uricosuric agent, a xanthine oxidase inhibitor, a weight reducing drug obese, alchoholics, being treated for leukemia with chemotherapy, patients with renal failure, patients with HGPRT deficience.

9. Primary center of ossification

Stimulated

Stimulated

Perchondrium

PTHrP

Brake

Syndergistic with

Stimulates

PTHrP receptor

Overgrowth

Rickets

Increased

Decreased

Decreased

Activating mutations of the FGFR3 receptor, inactivating mutations of the PTHrP receptor.

10. Kidneys are responsible for the coversion of 25-OH-vitD to 1,25-diOH-vitD, which is the active form. Vitamin D both increases intestinal absorbtion, and serves as a cofactor for PTH enhancing calcium resorption. So, lack of active vitamin D prevents calcium absorption and resorption of bone, leading to low serum levels of calcium.

This is similar to osteomalacia in adults and children respectively. This could be treated by administering active vit D in the form of 1,25 diOH vitD

- 11. Low vitamin D leads to hypocalcemia. Since calcium is the primary regulator of PTH levels by feedback inhibition, hypocalcemic plasma will lead to high levels of PTH. PTH will lead to increased phosphorus excretion by the kidney, and therefore low serum phosphate. Urine calcium will remain relatively unchanged, but slightly reduced.
- 12. Age suggests osteoporisis (highest risk, most likely). Type I v type II can be determined by radiographs. Relative progression/existence can be revealved by DXR. Osteomyolytis unlikely due to age (and lack of other underlying conditions such as DM, HIV etc., but culture to see if infectious agent can be found.

Traums – get hx

Metastatic cancer: breast (prostate not so likely) – hx, radiograph, biopsy Osteomalacia – (vitD deficiency) biopsy, blood sample, renal function (could be secondary to renal failure)

Hyperparathyroidism: blood levels of PTH, calcium, vit D

Theoretically (but not likely): inborn error (osteogenesis imperfect, osteopetrosis etc. but not likely due to age and location, likely eliminated by hx), Paget's (not likely due to location, DXR. Hx of other fracture, radiograph to eliminate).

13 and 14 – you've already had these on the pset.