Lippincott pathology questions 5

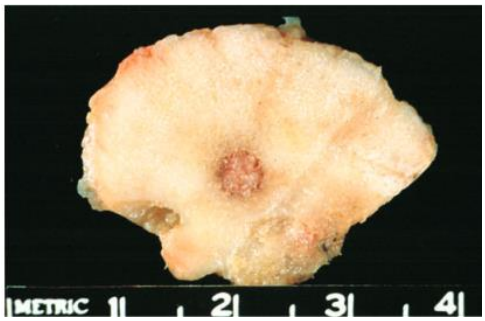
1) A 50-year-old woman presents with lower back pain of 3 weeks in duration. Radiologic studies reveal several discrete lytic lesions in the lumbar back and pelvis. Laboratory studies show elevated serum levels of alkaline phosphatase. Serum calcium, serum protein, and peripheral blood smears are normal. Aspiration biopsy of a pelvic lesion shows keratin-positive cells. Which of the following is the most likely diagnosis?

(A) Chondrosarcoma
(B) Metastatic carcinoma
(C) Osteochondroma
(D) Osteosarcoma
(E) Plasmacytoma

2) An 18-year-old man presents with bone pain about his knee that he has had for 6 weeks. Radiologic studies reveal a lytic lesion of the distal end of the femur, which arises in the metaphysis, extends into the proximal diaphysis, and elevates the periosteum. Serum levels of alkaline phosphatase are markedly elevated. The lesion is removed, and the cut surface of the surgical specimen is shown in the image. Molecular studies of this tumor would most likely reveal a mutation in the gene encoding which of the following proteins?

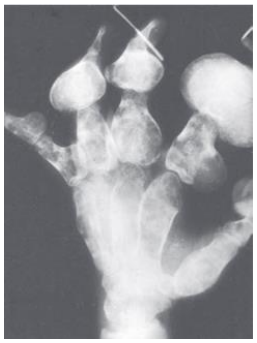
(A) Cyclin A
(B) Cyclin D
(C) Fibroblast growth factor receptor
(D) Rb tumor suppressor protein
(E) Stimulatory guanine nucleotide–binding protein

3) A 16-year-old boy presents with a 2-week history of pain in his right leg. He says that he has been taking aspirin to relieve the pain. An X-ray of the leg shows a 1-cm sharply demarcated, radiolucent lesion in the diaphysis of the tibia surrounded by dense, sclerotic bone. The lesion is surgically removed, and the gross specimen is shown in the image. Microscopically, the tumor shows irregular trabeculae of woven bone surrounded by osteoblasts, osteoclasts, and fibrovascular marrow. What is the appropriate diagnosis?



(A) Chondroblastoma
(B) Giant cell tumor of bone
(C) Osteoblastoma
(D) Osteoid osteoma
(E) Solitary chondroma

4) A 35-year-old woman has multiple cartilaginous lesions in her long and short bones. A radiograph of the hand (shown in the image) reveals bulbous swellings. A biopsy shows abnormally arranged hyaline cartilage, with scattered zones of proliferation. This patient is at risk for which of the following bone diseases?



(A) Chondrosarcoma
(B) Giant cell tumor of bone
(C) Osteosarcoma
(D) Histocytic lymphoma
(E) Synovial sarcoma

Answers:

1) B: Metastatic carcinoma. Multiple lytic lesions associated with keratin-positive cells strongly suggest meta-static bone cancer. Metastatic carcinoma is the most common tumor of bone, and skeletal metastases are found in at least 85% of cancer cases that have run their full clinical course. The vertebral column is the most commonly affected bony structure. Tumor cells usually arrive in the bone by way of the bloodstream. Some tumors (thyroid, gastrointestinal tract, kidney, neuroblastoma) produce mostly lytic lesions. A few neoplasms (prostate, breast, lung, stomach) stimulate osteo-blastic components to make bone. The other choices are not keratin positive.Diagnosis: Metastatic bone cancer

2) D: Rb tumor suppressor protein. Osteosarcoma is a highly malignant bone tumor characterized by formation of bone tissue by tumor cells. It is most frequent in adolescents between the ages of 10 and 20 years. Almost two thirds of cases of osteosarcoma exhibit mutations in the retinoblastoma (Rb) gene, and many tumors also contain mutations in p53. Often, the periosteum produces an incomplete rim of reactive bone adjacent to the site where it is lifted from the cortical surface by the tumor. When this appears on an X-ray as a shell of bone intersecting the cortex at one end and open at the other end, it is referred

to as Codman triangle. A "sunburst" periosteal reaction is often superimposed. Mutations in the fibroblast growth factor receptor gene (choice C) are a cause of achondroplasia. Deregulation of cyclins (choices A and B) and cyclin-dependent kinases are associated with several neoplasms.
Diagnosis: Osteosarcoma

3) D: Osteoid osteoma. Osteoid osteoma is a small, painful, benign lesion of bone composed of osseous tissue (the nidus) and surrounded by a halo of reactive bone formation. The tumor typically occurs in young persons ranging in age from 5 to 25 years. Osteoid osteoma frequently arises in the cortex of the diaphysis of the tubular bones of the lower extremity. Osteoid osteoma is a spherical, hyperemic tumor of about 1 cm in diameter that is considerably softer than the surrounding bone and easily enucleated at surgery. Reactive, sclerotic bone surrounds the nidus. Chondroblastoma (choice A) features primitive chondroblasts and cartilage matrix. Giant cell tumor (choice B) of bone is a locally aggressive neoplasm composed of multinucleated, osteoclastic giant cells. Osteoblastoma (choice C) is a benign neoplasm that is histologically similar to osteoid osteoma but larger and not accompanied by nocturnal pain relieved by aspirin. Solitary chondroma (choice E) is a benign, intraosseous tumor composed of well-differentiated hyaline cartilage.
Diagnosis: Osteoid osteoma

4) A: Chondrosarcoma. Enchondromatosis, also termed Ollier disease, is a bone disorder characterized by the development of numerous cartilaginous masses that lead to bony deformities. The condition is not strictly a disease of delayed maturation of bone, but one in which residual hyaline cartilage, anlage cartilage, or cartilage from the growth plate does not undergo endochondral ossifi cation and remains in the bones. As a consequence, the bones show multiple, tumor-like masses of abnormally arranged hyaline cartilage (enchondromas), with zones of proliferative and hypertro-phied cartilage. Enchondromas exhibit a strong tendency to undergo malignant change into chondrosarcomas in adult life. None of the other choices are related to cartilaginous tumors.
Diagnosis: Enchondromatosis, Ollier disease

Lippincott pathology questions 4

1) A 17-year-old girl suffers a spiral fracture of her right tibia, and the leg is casted. Unfortunately, the fracture does not heal correctly due to excessive motion and interposition of soft tissue at the fracture site. Which of the following represents the most likely complication of nonunion in this patient?

(A) Codman triangle formation
(B) Cup-shaped epiphysis
(C) Involucrum formation
(D) Osteomyelitis
(E) Pseudoarthrosis

2) A 10-year-old boy complains of increasing pain in his left hip. He began limping shortly after playing a baseball game at school. He is afebrile. An X-ray of the femoral head shows a fracture and irregular densities of the cancellous bone. You make a diagnosis of Legg-Calvé-Perthes disease. Which of the following best describes the pathologic findings in this patient?

(A) Avascular osteonecrosis
(B) Chondroma
(C) Fibrous dysplasia
(D) Osteitis fibrosa cystica
(E) Osteopetrosis

3)A 50-year-old man presents with a 2-day history of left leg pain. His temperature is 38.7°C (103°F). He has a harsh systolic murmur and echocardiographic evidence of bacterial endocarditis. If this patient has developed hematogenous osteomyelitis, his bone infection would most likely be found in which of the following anatomic locations?

(A) Body of a flat bone
(B) Diaphysis of a long bone
(C) Epiphysis of a long bone
(D) Metaphysis of a long bone
(E) Periosteum of a long bone

4) A 9-year-old boy complains of 2 weeks of pain in the hip. His temperature is 38°C (101°F). Laboratory studies show an elevated erythrocyte sedimentation rate. An X-ray reveals a mottled radiolucent defect in the upper femur, with abundant periosteal new bone formation. Fine-needle aspiration returns numerous neutrophils and cocci. Staphylococcus aureus is cultured from the bone lesion. A biopsy shows a fragment of necrotic bone embedded in fibrinopurulent exudate. Which of the following terms best describes the necrotic bone?

(A) Brodie abscess
(B) Cloaca
(C) Involucrum
(D) Osteophyte
(E) Sequestrum

Answers:

1) E: Pseudoarthrosis. If a fracture site does not heal, the condition is termed nonunion. Causes of non-union include interposition of soft tissues at the fracture site, excessive motion, infection, poor blood supply, and other factors mentioned in the question. Continued movement at the unhealed fracture site may also lead to pseudoarthrosis, a condition in which joint-like tissue is formed. In such cases, the fracture never heals, and the joint-like material must be removed

surgically for the fracture to heal properly. Codman triangle (choice A) is an X-ray fi nding of a bone involved in osteosarcoma, where, an incomplete rim of reactive bone adja-cent to tumor is lifted from the cortical surface. Involucrum (choice C) is the viable bone that surrounds necrotic bone (sequestrum) in osteomyelitis. Osteomyelitis (choice D) is an uncommon complication of a closed fracture.
Diagnosis: Nonunion of healing fracture

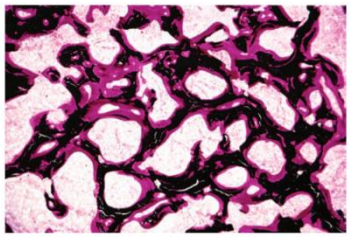
2) A: Avascular osteonecrosis.Osteonecrosis, also known as avascular necrosis, refers to the death of bone and marrow in the absence of infection. Such bone infarcts may be caused by a variety of conditions, such as trauma, thrombi, emboli, and corticosteroids. Growing bones of children and adolescents are often affected, and in most instances, the cause of such infarctions is not evident. Legg-Calvé-Perthes disease refers to osteonecrosis in the femoral head in children. Collapse of the femoral head may lead to joint incongruity and severe osteoarthritis. Chondroma (choice B) is a benign, intraosseous tumor composed of well-differentiated hyaline cartilage. Fibrous dysplasia (choice C) is a developmental abnormality of the skeleton, characterized by a disorganized mixture of fi brous and osseous elements in the interior of the affected bones. Osteitis fi brosa cystica (choice D) occurs in primary hyperparathyroidism.
Diagnosis: Avascular osteonecrosis

3) D: Metaphysis of a long bone.Hematogenous osteomyelitis primarily affects the metaphyseal area of the long bones (knee, ankle, hip) because of the unique vascular supply in this region. Normally, arterioles enter the calcifi ed portion of the growth plate, form a loop, and then drain into the med-ullary cavity without establishing a capillary bed. This vascu-lar loop permits slowing and sludging of blood fl ow, allowing bacteria time to penetrate the walls of the blood vessels and establish an infective focus within the bone marrow. Osteo-myelitis may break into the periosteum (choice E) but does not originate there. Vascular loops do not reach the epiphysis (choice C). Choices A and B would be distinctly uncommon.
Diagnosis: Osteomyelitis

4) E: Sequestrum.Infectious organisms may reach the bone through the bloodstream. If the infection is not contained, pus and bacteria extend into the endosteal vascular channels that supply the cortex and spread through-out the Volkmann and Haversian canals of the cortex. Even-tually, pus forms underneath the periosteum, shearing off the perforating arteries of the periosteum and further devitaliz-ing the cortex. This expansion may shear off the perforating arteries that supply the cortex with blood, leading to necro-sis of the cortex. The necrotic bone is called a sequestrum. Brodie abscess (choice A) consists of reactive bone from the periosteum and the endosteum that surrounds and con-tains the infection. Cloaca (choice B) is the hole found in the bone during formation of a draining sinus. Involucrum (choice C) refers to a lesion in which periosteal new bone formation forms a sheath around the necrotic sequestrum. Osteophytes (choice D) are bone nodules appearing on the peripheral portion of the joint surface that are complications of osteoarthritis.
Diagnosis: Osteomyelitis

Lippincott pathology questions 3

1) A 33-year-old woman presents with a spontaneous fracture of her femoral head. She has suffered from Crohn disease for 20 years. Multiple surgical procedures have resulted in the removal of much of her small bowel. She has had profound weight loss over the last 10 years. The bone is pinned. Histologically, the resected femoral head shows bony trabeculae that are covered by a thicker-than-normal layer of osteoid (shown in the image). In this section, the osteoid is stained red, and mineralized bone is stained black. Which of the following best describes the pathogenesis of this lesion?



(A) Degenerative changes in the subchondral bone
(B) Enhanced osteoblast activity
(C) Impaired mineralization of osteoid
(D) Inflammatory synovium with pannus formation
(E) Subperiosteal bone resorption

2) A 55-year-old man presents with pain in the left arm. Laboratory studies show elevated serum levels of calcium and parathyroid hormone. An X-ray of the left arm reveals multiple small bone cysts and pathologic fractures. Biopsy of the affected bone discloses numerous giant cells in a cellular and fibrous stroma. The patient undergoes removal of a parathyroid adenoma. Which of the following best describes the pathogenesis of bone pain and pathologic fractures in this patient?

(A) Enhanced osteoblast activity
(B) Impaired mineralization of osteoid
(C) Increased bone resorption
(D) Increased mineralization of bone
(E) Osteoporosis

3) A 67-year-old man from England develops bow-legs and leg pain over a period of 5 years. He also complains of progressive hearing loss over the last 2 years. A bone biopsy shows a mosaic pattern with prominent cement lines and increased osteoblastic and osteoclastic activity. Serum electrolyte levels are normal. This patient is at increased risk for developing which of the following diseases?

(A) Amyloidosis
(B) Multiple myeloma
(C) Osteogenic sarcoma
(D) Pulmonary embolism
(E) Renal failure

Answers:

1) C: Impaired mineralization of osteoid. Osteomalacia (soft bones) is a disorder of adults characterized by inadequate mineralization of newly formed bone matrix. Diverse conditions associated with osteomalacia and rickets include abnormalities in vitamin D metabolism, phosphate defi ciency states, and defects in the mineralization process itself. In osteomalacia, the bony trabeculae are rimmed by broad layers of osteoid, whereas the bone spicules in osteoporosis are thin but normally mineralized. Intrinsic diseases of the small intes-tine, cholestatic disorders of the liver, biliary obstruction, and chronic pancreatic insuffi ciency are the most frequent causes of osteomalacia in the United States. Malabsorption of vita-min D and calcium complicates a number of small intestinal diseases, including celiac disease, Crohn disease, and sclero-derma. Enhanced osteoblast activity (choice B) is encountered in new bone formation. Inflammatory synovium with pannus formation (choice D) is a feature of rheumatoid arthritis.

Diagnosis: Osteomalacia

2) C: Increased bone resorption. In patients with primary hyperparathyroidism, osteoclasts are stimulated to resorb bone. From the subperiosteal and endosteal surfaces, osteoclasts bore their way into the cortex as cutting cones. This process is termed dissecting osteitis. As the disease progresses, the trabecular bone is resorbed, and the marrow is replaced by loose fibrosis. Cystic degeneration ultimately occurs, leading to areas of fibrosis that contain reactive woven bone, and hemosiderin-laden macrophages often dis-play many giant cells, which are actually osteoclasts. Because of its macroscopic appearance, this lesion has been termed a brown tumor. This is not a true tumor, but rather a repair reaction. Impaired mineralization of osteoid (choice B) is a feature of osteomalacia. Osteoporosis (choice E) is characterized by decreased but otherwise normally mineralized bone. Diagnosis: Hyperparathyroidism, osteitis fibrosa cystica

3) C: Osteogenic sarcoma. Paget disease is a chronic condition characterized by lesions of bone resulting from disordered remodeling, in which excessive bone resorp-tion initially results in lytic lesions, followed by disorganized and excessive bone formation. The diagnostic hallmark in late disease is an abnormal arrangement of lamellar bone, in which islands of irregular bone formation, resembling pieces of a jig-saw puzzle, are separated by prominent cement lines. Persons of English descent have a high incidence of this disease. Neo-plastic transformation may occur in a focus of Paget disease, usually in the femur, humerus, or pelvis. This complication occurs in less than 1% of all cases; however, the incidence of osteogenic sarcoma is still 1,000 times higher than that in the general population. The other choices are not associated with disorganized bone. Diagnosis: Paget disease, osteogenic sarcoma

Lippincott pathology questions 2

1) A 24-year-old man on chronic corticosteroid therapy for severe asthma presents with a 6-month history of increasing hip pain. This patient most likely exhibits symptoms of which of the following metabolic bone diseases?

(A) Gaucher disease
(B) Osteomalacia
(C) Osteopetrosis
(D) Osteoporosis
(E) Paget disease

2) A 30-year-old man with dwarfism is admitted to the hospital for hip replacement due to severe osteoarthritis. He has short arms and legs and a relatively large head. His parents do not show signs of this congenital disease. This patient most likely has a spontaneous mutation in the gene encoding which of the following proteins?

(A) Collagen type I
(B) Dystrophin
(C) Fibroblast growth factor receptor
(D) Growth hormone receptor
(E) Insulin-like growth factor

3)A 2-year-old boy is treated for recurrent fractures of his long bones. Physical examination reveals blue sclerae, loose joints, abnormal teeth, and poor hearing. Molecular diagnostic studies will most likely demonstrate a mutation in the gene encoding which of the following proteins?

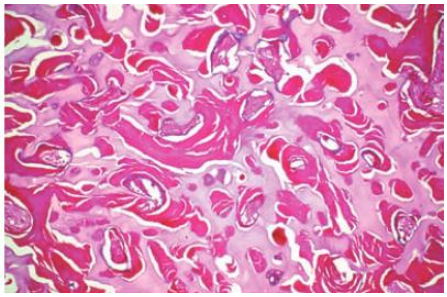
(A) Collagen
(B) Dystrophin
(C) Lysyl hydroxylase
(D) Fibrillin
(E) Fibroblast growth factor receptor

4) A 58-year-old woman fractures her hip after slipping on an icy sidewalk. An X-ray shows generalized osteopenia. A bone biopsy reveals attenuated bony trabeculae and a normal ratio of mineral-to-matrix. Serum calcium and phosphorus levels are normal. Which of the following best explains the pathogenesis of osteopenia in this postmenopausal woman?

(A) Impaired mineralization of osteoid
(B) Increased osteoblast activity
(C) Increased mineralization of bone
(D) Increased osteoclast activity
(E) Mosaic bone formation

5) A 6-year-old child with mild hydrocephalus suffers chronic infections and dies of intractable chronic anemia. At autopsy, his bones are dense and misshapen. The femur, in particular, shows obliteration of the marrow space. Histologically, the bones demonstrate disorganization of bony trabeculae by retention of primary spongiosa and further obliteration of the marrow spaces by secondary spongiosa (shown in the image). Hematopoietic bone marrow cells are sparse. The disorder is caused by mutations in genes that regulate which of the following cell types?

(A) Fibroblasts
(B) Myofibroblasts
(C) Normoblasts
(D) Osteoblasts
(E) Osteoclasts



Answers:

1) **D: Osteoporosis.** Risk factors for osteoporosis include smoking, vitamin D deficiency, low body mass index, hypogonadism, a sedentary lifestyle, and glucocorticoid therapy (seen in this patient). Bone loss and fractures are the hallmarks of osteoporosis, regardless of the underly-ing cause. Choices A and C are congenital disorders that are not related to corticosteroid therapy. Choices B and E are acquired conditions but they are not related to corticosteroid therapy.
Diagnosis: Osteoporosis

2) **C: Fibroblast growth factor receptor.** Achondroplasia refers to a syndrome of short-limbed dwarfi sm and macrocephaly and represents a failure of normal epiphyseal cartilage formation. It is the most common genetic form of dwarfism and is inherited as an autosomal dominant trait. However, most cases represent new mutations. Achondroplasia is caused by an activating mutation in the fibroblast growth factor-3 receptor. This mutation negatively regulates chondrocyte proliferation and differentiation and arrests the development of the growth plate. A defective growth hormone receptor (choice D) is responsible for rare cases of dwarfism (Laron dwarfism). Mutations in dystrophin (choice B) are encountered in cases of Duchenne muscular dystrophy. Congenital deficiency of insulin-like growth factor (choice E) has not been reported as a cause of achondroplasia.
Diagnosis: Achondroplasia

3) **A: Collagen.** Osteogenesis imperfecta (OI) refers to a group of mainly autosomal dominant, heritable disorders of connective tissue, caused by mutations in the gene for type I collagen; this affects the skeleton, joints, ears, ligaments, teeth, sclerae, and skin. The pathogenesis of OI involves mutations of COL1A1 and COL1A2 genes, which encode the a1 and a2 chains of type I procollagen, the major structural protein of bone. Mutations in lysyl hydroxylase gene (choice C) are seen in patients with Ehlers-Danlos syndrome, and mutations in the fi brillin gene (choice D) account for Marfan syndrome. Mutations in the dystrophin gene (choice B) cause Duchenne muscular dystrophy. Mutations in the fi broblast growth factor receptor gene (choice E) may result in achondroplasia.
Diagnosis: Osteogenesis imperfecta

4) **D: Increased osteoclast activity.** Osteoporosis is a metabolic bone disease characterized by diffuse skeletal lesions in which normally mineralized bone is decreased in mass to the point that it no longer provides adequate mechanical support. The remaining bone exhibits a normal ratio of mineralized to non-mineralized (osteoid) matrix (therefore, not choices A and C). Bone loss and eventually fractures are the hallmarks of osteoporosis. Primary osteoporosis occurs principally in postmenopausal women (type 1) and elderly persons of both sexes (type 2). Type 1 primary osteoporosis is due to an absolute increase in osteoclast activity. The increased number of osteoclasts that appear in the early postmenopausal skeleton is the direct result of estrogen withdrawal. Type 2 osteoporosis reflects decreased osteoblast activity (therefore, not choice B). Mosaic bone formation (choice E) is a feature of Paget disease.
Diagnosis: Osteoporosis, osteopenia

Note that we don't depend on serum calcium or phosphate for diagnosis (Robbins)

5) **E: Osteoclasts.** Osteopetrosis, also known as "marble bone" disease or Albers-Schönberg disease, is a group of rare, inherited disorders. The most common autosomal recessive form is a severe, sometimes fatal dis-ease affecting infants and children. The sclerotic skeleton of osteopetrosis is the result of failed osteoclastic bone resorption. The disease is caused by mutations in genes that govern osteoclast formation or function. Because osteoclast function is arrested, osteopetrosis is characterized by (1) the retention of the primary spongiosum with its cartilage cores, (2) lack of funnelization of the metaphysis, and (3) a thick-ened cortex. The result is short, block-like, radiodense bones, and hence the term marble bone disease. Choices A, B, and C do not regulate bone organization. Increased osteoblast activity (choice D) has not been demonstrated in patients with osteopetrosis.
Diagnosis: Osteopetrosis, Albers-Schönberg disease