A 70-year-old man is experiencing neck pain, progressive weakness, and numbness in his arms and legs without bowel or bladder dysfunction or dysphagia. Upon examination, he has atrophy of his upper extremities but normal muscle bulk in his legs. Strength is diffusely 4/5 throughout. Cervical spine radiographs show spondylosis. Electromyography (EMG) reveals fibrillations with increased amplitude in the extensor carpi radialis and pronator teres. Nerve conduction studies demonstrate slowing conduction diffusely in the sural, peroneal, and ulnar nerves, and severe slowing in the median nerve. Testing of the tongue and thoracic paraspinal muscles does not show fibrillations or positive short waves. What is the most likely diagnosis?

1- Amyotrophic lateral sclerosis  
2- Cubital tunnel syndrome  
3- Normal aging  
4- Cervical radiculopathy

PREFERRED RESPONSE: 4- Cervical radiculopathy

DISCUSSION

Physical examination and presentation is consistent with possible cervical radiculopathy vs motor neuron disease. EMG findings are most consistent with cervical radiculopathy. There is denervation (fasciculations and positive short waves) of the C6 innervated muscles consistent with radiculopathy. However, evaluation of other body regions does not show evidence of denervation (tongue, thoracic paraspinal muscles). Fasciculations in the hand muscles were not widespread. Nerve conduction suggests the presence of a peripheral polyneuropathy with possible superimposed median neuropathy. Amyotrophic lateral sclerosis is a motor neuron disease that affects both upper and lower neurons. Presentation includes rapid progression of weakness, muscle atrophy, fasciculations, spasticity, dysarthria, dysphagia, and respiratory compromise.
**Question 2 of 100**

Sclerostin and dickkopf-1 (Dkk-1) are direct inhibitors of what pathway related to bone and/or cartilage regulation?

1- Bone morphogenetic protein (BMP)/SMAD pathway  
2- Receptor activator of nuclear factor kappa beta (RANK)/RANK ligand (RANKL) pathway  
3- Wnt/Beta-catenin (β-catenin) pathway  
4- Parathyroid hormone (PTH) pathway

PREFERRED RESPONSE: 3- Wnt/Beta-catenin (β-catenin) pathway

**DISCUSSION**

Dkk-1 and sclerostin are proteins that inhibit the binding of the Wnt molecule to receptors LRP5/6. In the absence of sclerostin and Dkk-1, Wnt binds to its receptor, which in turn inhibits phosphorylation of the β-catenin. The unphosphorylated β-catenin then builds up in the cytoplasm of the cell, allowing it to be transported to the nucleus of the cell. Once in the nucleus, β-catenin will lead to upregulation of a series of proteins involved in osteoblast formation differentiation. Knocking out or inhibiting sclerostin or Dkk-1 results in increased bone mass secondary to constitutive activation of the Wnt/β-catenin pathway. The other responses are not directly affected by Dkk-1 or sclerostin. RANKL and RANK are expressed on osteoblasts and osteoclasts, respectively, and are involved in osteoblast-mediated osteoclast activation. BMPs work through SMADs to cause osteoblastic differentiation, and there is reported crosstalk between the Wnt and BMP pathways (but this is an indirect link). Finally, PTH at physiologic levels binds to osteoblasts, causing a series of events that lead to osteoblast-mediated osteoclast activation and subsequent increased bone resorption.
RESPONSES FOR QUESTIONS 3 THROUGH 6

1- Adhesive wear
2- Abrasive wear
3- Fatigue wear
4- Delamination

For each scenario below, please choose the most likely dominant mechanism of wear from the list above.

**Question 3 of 100**

A well-functioning total hip arthroplasty

1- Adhesive wear
2- Abrasive wear
3- Fatigue wear
4- Delamination

PREFERRED RESPONSE: 1- Adhesive wear

**Question 4 of 100**

A total hip arthroplasty in which the femoral head was scratched during the final reduction

1- Adhesive wear
2- Abrasive wear
3- Fatigue wear
4- Delamination

PREFERRED RESPONSE: 2- Abrasive wear

**Question 5 of 100**

A total knee arthroplasty in which the polyethylene was sterilized with gamma radiation in air

1- Adhesive wear
2- Abrasive wear
3- Fatigue wear
4- Delamination

PREFERRED RESPONSE: 4- Delamination

**Question 6 of 100**

A total knee arthroplasty revision in which several small cement particles have entered the articulation
1- Adhesive wear
2- Abrasive wear
3- Fatigue wear
4- Delamination

PREFERRED RESPONSE: 2- Abrasive wear

DISCUSSION

Adhesive wear occurs when 2 surfaces are forced together under a load experience motion. When the adhesive forces exceed the material strength, material is removed from the weaker material. Adhesive wear is the most common mechanism seen in well-functioning hips. Abrasive wear occurs under 2 modes: two-body and three-body abrasive wear. Two-body abrasive wear occurs when asperites or projections from 1 surface remove material from the opposed articulating surface. This is seen with a roughened or damaged surface such as a scratched femoral head. Three-body wear occurs when a third body particle is interposed between the bearing surfaces and results in removal of material from 1 or both of the articular surfaces. Delamination is a type of surface damage seen with oxidized polyethylene. Delamination is frequently seen in knees as a result of crossing wear patterns and high-contact stresses. Fatigue wear occurs when surface and subsurface cyclic shear stresses or strains in the softer material of an articulation exceed the fatigue limit for that material.
A 62-year-old woman has advanced osteoarthritis of the knee that has been refractory to nonsurgical treatment. She wishes to discuss total knee arthroplasty. She reports a lifelong history of intolerance to most jewelry and is concerned about having an allergic reaction to the metallic knee implant. Hypersensitivity to metal implants is usually classified as what type of Gell-Coombs reaction?

1- I (allergic)
2- II (cytotoxic, antibody-dependent)
3- III (immune complex)
4- IV (delayed type)

PREFERRED RESPONSE: 4- IV (delayed type)

DISCUSSION

Most "metal allergy" is classified as type IV, or delayed-type hypersensitivity response, which is a cell-mediated response. Types I, II, and III are not generally associated with metal hypersensitivity responses. Type I reactions are typically anaphylaxis. Type II reactions are antibody mediated, such as seen in Grave's disease or hemolytic anemia. Type III reactions are immune complex diseases such as serum sickness or systemic lupus erythematosus.
A surgeon decides to report outcomes for a new surgical procedure that he has performed on 10 patients who have a rare type of arthritis. He provides data on the functional and subjective patient outcomes. This type of study design is best described as...

1- case series.
2- case-control study.
3- cohort study.
4- randomized clinical trial.

PREFERRED RESPONSE: 1- case series.

DISCUSSION

The type of study design in which a series of cases is presented with outcomes (without a control population or comparison group) is known as a case series. This type of study design, although frequently seen in orthopaedic literature, provides the lowest level of evidence. There is no control group and the population is usually poorly defined. This type of study can be helpful as a starting point for further analysis. A randomized trial provides the highest level of evidence in medical research, featuring a comparison group and randomized (and usually blinded) placement of subjects into study groups. In case-control studies, cases are compared to a control group. The control group has not been randomized, but may be a naturally occurring group of subjects who have not had the same exposure or intervention as the case group. A cohort study can be retrospective or prospective and usually looks at a large group of people over time to assess exposures and incidence of disease.
**Question 9 of 100**

A study is proposed in which 2 groups of patients are randomized to treatment with bisphosphonates or placebo. This is an example of what study type?

1- Crossover design trial  
2- Parallel design trial  
3- Cohort study  
4- Case series

PREFERRED RESPONSE: 2- Parallel design trial

**DISCUSSION**

In a parallel design trial, participants are randomized to 2 or more groups, each of which receives a different treatment or intervention. For example, Group A receives the drug and Group B receives the placebo. This type of design allows for comparison between groups. In a crossover design clinical trial, both groups receive both interventions over a defined time period. For example, Groups A and B both receive the drug as well as the placebo. This allows for within-participant comparisons. In a cohort study, patient groups are followed over time on the basis of having or not having received an exposure. Cohort studies are not randomized. In a case series, patients often receive a particular treatment and the outcomes are then examined.
A 5-year-old boy has a history of delayed walking and difficulty climbing stairs. Physical examination shows a positive Gower sign and scoliosis. Laboratory tests show elevated serum creatine phosphokinase. A mutation of what protein results in this disorder?

1- Dystrophin
2- Collagen type I
3- Neurofibromin
4- Runt-related transcription factor 2 (Runx2)

PREFERRED RESPONSE: 1- Dystrophin

DISCUSSION

Duchenne muscular dystrophy (DMD) is an X-linked muscular disorder that affects boys between 3 and 6 years of age. Clinically, symptoms include delayed walking and difficulty climbing stairs. DMD is caused by mutations of the dystrophin gene. Patients are often found to have Gower and Trendelenburg signs with proximal muscle weakness. Serum creatine phosphokinase is often elevated and the diagnosis can be made with dystrophin staining from muscle biopsy specimens. Runx2 mutations are associated with cleidocranial dysplasia, a disorder of membranous ossification with hypoplasia or absence of the clavicle and widening of the symphysis pubis. Mutations of collagen type I are most often associated with osteogenesis imperfecta. Neurofibromin is the protein product of the NF-1 gene that is associated with neurofibromatosis.
After sustaining a muscle contusion injury, prolonged immobilization leads to

1. increased tensile stiffness.
2. increased granulation tissue production.
3. improved recovery of tensile strength.
4. reduced incidence of myositis ossificans.

PREFERRED RESPONSE: 2- increased granulation tissue production.

DISCUSSION

Increased granulation tissue production occurs with prolonged immobilization following contusion injury; this condition may lead to myositis ossificans. Prolonged immobilization can lead to contraction of scar, poor structural organization of the regenerating muscle, and, ultimately, scar tissue. In a study by Järvinen and associates, muscles immobilized following contusion injury were pulled to failure at tensile strengths much lower than tolerated by mobilized limbs. In addition, there is a decrease in tensile stiffness.
Delayed-onset muscle soreness (DOMS) is initially evident at the muscle tendon junction and can spread throughout the entire muscle. It is primarily associated with what type of exercise?

1- Concentric  
2- Isometric  
3- Eccentric  
4- Plyometric  

PREFERRED RESPONSE: 3- Eccentric

DISCUSSION

DOMS is primarily associated with eccentric exercise because fiber lengthening occurs during muscle contraction. Muscle injury occurs very early during eccentric exercise, with structural disruption of the cytoskeleton. A significant increase in creatine kinase levels occurs 24 to 48 hours after exercise and may peak between 3 to 6 days after exercise. All other choices are not strongly associated with delayed muscle soreness.
Question 13 of 100

Figures 13a and 13b are the radiograph and biopsy specimen of a 72-year-old woman who had increasing thigh pain for several months. She fell at home and was suddenly unable to bear weight on her right side. What is the most appropriate diagnostic test?

1- Chest CT scan  
2- CT scans of the chest, abdomen, and pelvis  
3- Serum protein electrophoresis (SPEP), urine protein electrophoresis (UPEP), and skeletal survey  
4- Renal ultrasound

PREFERRED RESPONSE: 1- Chest CT scan

DISCUSSION

The radiograph shows a pathologic fracture through a destructive lesion within the femoral canal that has cartilaginous components. The biopsy specimen confirms the presence of high-grade chondrosarcoma. The preferred response is a chest CT scan. CT scans of the abdomen and pelvis are unnecessary for the workup of bone sarcomas because these sarcomas rarely metastasize to visceral organs. Their primary site of metastasis is the lungs. An MRI scan of the right femur, as well as a bone scan, are essential parts of the workup for a patient with a sarcoma. Renal ultrasound plays no role in the workup for this patient. SPEP, UPEP, and skeletal survey would be part of a workup for multiple myeloma, not chondrosarcoma.
Question 14 of 100

A 23-year-old man was a restrained backseat passenger in a head-on motor vehicle collision. Examination revealed extensive bruising diagonally across his chest and abdominal areas and extreme pain at the thoracolumbar junction posteriorly. The lateral chest radiograph showed splaying of the spinous processes and increased disk height at the level of the injury, but no fracture of the vertebral bodies. He underwent a posterior spine fusion with instrumentation to stabilize the spine after a full trauma workup revealed the spine to be his only injury. Where is the center of rotation for this injury?

1- Interspinous ligaments  
2- Posterior longitudinal ligament  
3- Anterior longitudinal ligament  
4- Abdominal viscera

PREFERRED RESPONSE: 4- Abdominal viscera

DISCUSSION

The injury described is termed a "chance fracture" of the spine, and the radiograph suggests significant soft-tissue disruption of the spine without bony involvement anteriorly. The question asks the examinee to infer that the injury is an all-soft-tissue injury, continuing through the disk space, and that the forces acting on the spine are almost completely distractive and on the same side of the center of rotation. A chance fracture of the spine is classically regarded as a flexion-distraction injury resulting in variable bony/soft-tissue injury to the spine, classically associated with a center of rotation anterior to the spine (frequently being associated with bowel or other abdominal organ injury).
Question 15 of 100

Implants composed of polylactic acid are excreted by what system after they are absorbed?

1- Hepatic
2- Renal
3- Respiratory
4- Gastrointestinal

PREFERRED RESPONSE: 3- Respiratory

DISCUSSION

Polylactic acid suture and suture anchors are popular bioabsorbable orthopaedic implants. This material undergoes hydrolysis of the ester background in vivo. Resulting lactic acid enters the tricarboxylic acid (Krebs) cycle and is excreted as carbon dioxide by the lungs. Polyglycolic acid and poly(p-dioxanone) may also be excreted by the kidneys.
Question 16 of 100

What role does quorum sensing play in the development of a bacterial biofilm?

1- Activates genes that produce virulence factors
2- Creates planktonic bacteria
3- Facilitates bacterial adhesion to a substrate
4- Lowers antimicrobial resistance

PREFERRED RESPONSE: 1- Activates genes that produce virulence factors

DISCUSSION

The development of a bacterial biofilm is a 2-stage process. The first step is the adhesion of individual bacteria to a substrate regulated by adhesions. After several bacteria have attached, quorum sensing (cell-to-cell communication) allows maturation of the biofilm and expression of genes that activate virulence factors. This can also increase the antibacterial resistance of the bacteria. Planktonic bacteria are individual free-moving bacteria.
Question 17 of 100

A 14-year-old boy sustained a right forearm fracture after a moderate-speed fall while skateboarding. He was previously treated for fractures of his left femur and right tibia, all from low-energy mechanisms. He has had some mild vertigo since school age, but otherwise has had an unremarkable birth and growth history. His family history is significant for frequent fractures (his mother). On examination, he has slightly blue sclerae, grossly normal hearing, and normal dentition. Chest, abdomen, and pelvis radiographs reveal a mild curvature of the spine (Cobb angle 10 degrees) and suggestion of a slightly large aortic knob. Findings from a nonaccidental trauma workup were normal. This boy's bones are fragile because of a gene mutation affecting what protein?

1- Fibroblast growth factor receptor (FGFR)
2- Fibrillin
3- Collagen
4- Cartilage oligomeric matrix protein

PREFERRED RESPONSE: 3- Collagen

DISCUSSION

This patient exhibits characteristics of osteogenesis imperfecta caused by a collagen mutation. FGFR3 mutations are responsible for achondroplasia. Fibrin mutations are thought to cause Marfan syndrome. Cartilage oligomeric matrix protein mutations are found in patients with pseudoachondroplasia.
Question 18 of 100

A 5-year-old boy sustains a Salter-Harris type II fracture of the distal femur. One year later, he is noted to have radiographic evidence of injury. Injury to the physis occurred through which cellular layer?

1- Resting
2- Proliferative
3- Maturation
4- Lower hypertrophic

PREFERRED RESPONSE: 4- Lower hypertrophic

DISCUSSION

Most physeal fracture separations occur at the zone of hypertrophy or at the chondro-osseous junction. In Salter-Harris types III and IV fractures, the resting, proliferative, and upper hypertrophic zones are sometimes involved.
Question 19 of 100

A patient sustains a grade III medial collateral ligament injury. One year later, when compared to collagen in an uninjured ligament, an increase is likely in the

1- gross number of fibers.
2- proportion of type III fibers.
3- cross-linking.
4- mass and diameter of fibers.

PREFERRED RESPONSE: 1- gross number of fibers.

DISCUSSION

Studies on animal models have shown that there is a change in collagen fiber type and distribution early in the healing process. There is a higher portion of type III fibers than in normal ligament initially, but this ratio returns to normal about 1 year after the injury occurs. Healing ligaments show an increased number of collagen fibers, but the number of mature collagen cross-links is 45% of predicted value after 1 year. There is also a decrease in the mass and diameter of the collagen fibers.
Question 20 of 100

During endochondral ossification of the growth plate, the process that most contributes to the longitudinal growth of long bones is

1- chondrocyte apoptosis.
2- chondrocyte hypertrophy.
3- chondrocyte proliferation.
4- growth plate matrix synthesis.

PREFERRED RESPONSE: 2- chondrocyte hypertrophy.

DISCUSSION

The growth plate is divided into 5 distinct zones: reserve, proliferative, maturation, hypertrophy, and vascular invasion. During growth-plate chondrocyte hypertrophy, intracellular volume and an increase in chondrocyte height are responsible for most growth of long bones. Other factors that contribute to bone growth are chondrocyte proliferation and matrix synthesis, but to a lesser degree than chondrocyte hypertrophy. Growth plate chondrocytes undergo programmed cell death (apoptosis) after hypertrophy takes place.
A 32-year-old man who is a smoker sustained an open tibial fracture and underwent a staged treatment with placement of an intramedullary nail. Four weeks after surgery, he developed a pseudomonas deep-wound infection. What is the strongest predictor of persistent infection if implants are retained until fracture union?

1- Open fracture
2- Smoking history
3- Pseudomonas organism
4- Tibia fracture

PREFERRED RESPONSE: 1- Open fracture

DISCUSSION

Berkes and associates showed that in a single-center retrospective study of all patients treated with open reduction and internal fixation of extremity fractures that resulted in early postsurgical deep wound infections, the only variables that showed statistical significance were history of open fracture as the initial injury or use of an intramedullary nail. Smoking history, intraoperative cultures showing pseudomonas species, and involvement of the lower extremity were not significant. Rightmire and associates examined patients at longer follow up, and showed smoking to be a risk factor for clinical failure.
Question 22 of 100

The patient shown in Figures 22a and 22b has what defect or deficiency?

1- Fibroblastic growth factor receptor 3 (FGFR3)
2- Type II collagen (COL2A)
3- Core-binding factor alpha 1 (CBFA1)
4- Cartilage oligomeric protein (COMP)

PREFERRED RESPONSE: 4- Cartilage oligomeric protein (COMP)

DISCUSSION

The patient shown has findings consistent with pseudoachondroplasia, which is caused by a mutation in COMP. Patients have short stature (3.5-4.5 feet) and resemble achondroplastic dwarfs with rhizomelic proximal segments. Limbs are disproportionately short, with limitation of elbow extension. Radiographically, patient appearance is normal at birth but become severely abnormal with growth. Pseudoachondroplasia is distinguished from achondroplasia by multiple joint deformities and normal facies. FGFR3 mutation is found in achondroplasia and can be diagnosed at any age. Clinical features include short stature (adult height 4 feet), a long trunk, rhizomelic extremities, and dysmorphic facies (large head, frontal bossing, and depressed nasal bridge). COL2A gene mutation is found in spondyloepiphyseal dysplasias (ie, Kniest syndrome, Stickler syndrome, spondyloepiphyseal dysplasia congenital). This condition is usually evident at birth: facies with mild midface flattening, short necks, and barrel-shaped chests. At walking age, thoracolumbar kyphosis with excessive lordosis is evident. Mutation in CBFA1 is found in cleidocranial dysplasia presenting with hypo/aplasia of the clavicles, open skull
sutures with bulging calvarium, midface hypoplasia, wide symphysis pubis, mild-to-moderate short stature, and short middle phalanx of the little finger.
Question 23 of 100

Premature arrest following growth plate injury is attributed to what mechanism?

1- Proliferation of the perichondrial ring of LaCroix
2- Initiation of Wolff's law
3- Disruption of the Heuter-Volkmann principle
4- Vascular invasion across the physis

PREFERRED RESPONSE: 4- Vascular invasion across the physis

DISCUSSION

Salter-Harris types III and IV fractures create disruption through all physeal zones. A conduit for invasion of blood vessels not normally present between the metaphysis and epiphysis creates the potential for influx of osteoblasts and formation of a bony bar that prevents further longitudinal growth. The remaining responses do not contribute to traumatic physeal arrest. The perichondral ring of LaCroix is a fibrocartilagenous periosteal ring surrounding the physis that provides up to 50% of resistance to shear stress. According to Wolff's law, bone deposition and resorption occurs in response to the stresses placed upon it. The Heuter-Volkmann principle describes slowing of longitudinal physeal growth in response to increasing compressive force. The hypertrophic zone demonstrates a decrease in cell size and columnar density as physeal closure approaches.
Question 24 of 100

Bacterial resistance to tetracycline is confirmed by ribosome protection, tetracycline modification, and

1- altered RNA polymerase.
2- altered membrane binding protein.
3- increased drug efflux.
4- DNA gyrase mutation.

PREFERRED RESPONSE: 3- increased drug efflux.

DISCUSSION

Mutations of bacterial DNA gyrase can decrease the effectiveness of quinolones. Altered membrane-binding protein is observed with resistance to β-lactam antibiotics. Tetracyclines are antibiotics that inhibit bacterial growth by stopping protein synthesis. Three specific mechanisms of tetracycline resistance have been identified: increased tetracycline efflux, ribosome protection, and tetracycline modification. Alteration of RNA polymerase is found in resistance to rifampin.
RESPONSES FOR QUESTIONS 25 THROUGH 27

1- Radiation  
2- Ethylene oxide  
3- Remelting  
4- Annealing

Ultra-high-molecular-weight polyethylene (UHMWPE) is a commonly used polymer in total hip and knee replacement. Please refer to the list of terms above in reference to UHMWPE and select the most appropriate response to the questions below.

**Question 25 of 100**

What process has the most positive effect on the wear-resistance characteristics of UHMWPE?

1- Radiation  
2- Ethylene oxide  
3- Remelting  
4- Annealing

PREFERRED RESPONSE: 1- Radiation

**Question 26 of 100**

What process directly increases cross-linking?

1- Radiation  
2- Ethylene oxide  
3- Remelting  
4- Annealing

PREFERRED RESPONSE: 1- Radiation

**Question 27 of 100**

What process changes polyethylene from its partial crystalline state to its amorphous state?

1- Radiation  
2- Ethylene oxide  
3- Remelting  
4- Annealing

PREFERRED RESPONSE: 3- Remelting

DISCUSSION

UHMWPE is a long polyethylene polymer with a high molecular weight. It is manufactured via ram bar extrusion and compression molding. Radiation is used to
sterilize and cross-link. Historically, gamma was irradiated in air at 2.5-4.0 Mrad. This created free radicals, resulting in early oxidative degradation with high wear rates, delamination, and fracture. Modern UHMWPE is highly cross-linked with higher doses of radiation (5.0-10 Mrad) in an inert environment. The level of radiation directly increases the amount of cross-linking and also improves wear resistance via cross-linking. Free radicals are still generated during the radiation process and are quenched by either remelting or annealing. Remelting is the heating of the polyethylene above its melt point, changing it from the partial crystalline state to the amorphous state and removing all free radicals, but also reducing wear characteristics. In annealing, the UHMWPE is heated below the melting point, which avoids the reduction in crystallinity but leaves more free radicals. Ethylene oxide is used in the sterilization process. Highly cross-linked polyethylene has shown significantly decreased wear rates compared to conventional polyethylene in both clinical and simulator studies. There is still some concern regarding decreased mechanical properties.
Question 28 of 100

Patients with Friedreich ataxia are most likely to have what condition?

1- Hip dysplasia
2- Malignant hyperthermia
3- Foot deformity
4- Tibia vara

PREFERRED RESPONSE: 3- Foot deformity

DISCUSSION

Friedrich ataxia is a spinocerebellar disorder characterized by ataxic gait, areflexia, muscle weakness, loss of proprioception, scoliosis, and foot deformity. Foot deformity can consist of varus heel, cavus deformity, and claw toes. Hip dysplasia can be associated with Charcot-Marie-Tooth disease, a hereditary motor sensory neuropathy. Patients with Blount disease often have progressive tibia vara and associated femoral deformity. Malignant hyperthermia has been reported in patients with myelomeningocele.
What protein promotes tumor cell attachment to bone during metastasis?

1- Integrin
2- Interleukin-1 (IL-1)
3- Osteocalcin
4- Vascular endothelial growth factor

PREFERRED RESPONSE: 1- Integrin

DISCUSSION

Metastasis to bone occurs in several cancer types, including breast, lung, renal, thyroid, prostate, and others. When tumor cells lodge in the bone, a disruption of normal bone remodeling occurs, resulting in bone formation or osteolysis. Integrins are the most common cell adhesion molecule that promotes cell-to-cell or cell-to-matrix binding. Cancer cells with integrins that recognize matrix proteins in bone can facilitate attachment to bone. IL-1 is a cytokine that acts in a proinflammatory manner within the body and is produced mainly by macrophages. Osteocalcin is secreted by osteoblasts and plays a role in mineralization and calcium homeostasis. Vascular endothelial growth factors are pro-angiogenic proteins that increase vascularity during tumor growth and metastasis.
RESPONSES FOR QUESTIONS 30 THROUGH 34

1- Aminoglycosides  
2- Cephalosporins  
3- Glycopeptides  
4- Rifamycins  
5- Macrolides  
6- Fluoroquinolones

Match the mechanism of action below with the class of antibiotic listed above.

**Question 30 of 100**

Inhibits cell-wall production by preventing peptidoglycan cross-linkage

1- Aminoglycosides  
2- Cephalosporins  
3- Glycopeptides  
4- Rifamycins  
5- Macrolides  
6- Fluoroquinolones

PREFERRED RESPONSE: 2- Cephalosporins

**Question 31 of 100**

Inhibits cell-wall production by interfering with the addition of cell-wall subunits

1- Aminoglycosides  
2- Cephalosporins  
3- Glycopeptides  
4- Rifamycins  
5- Macrolides  
6- Fluoroquinolones

PREFERRED RESPONSE: 3- Glycopeptides

**Question 32 of 100**

Inhibits translation through irreversible binding of the 30S ribosomal subunit

1- Aminoglycosides  
2- Cephalosporins  
3- Glycopeptides  
4- Rifamycins  
5- Macrolides  
6- Fluoroquinolones

PREFERRED RESPONSE: 1- Aminoglycosides
**Question 33 of 100**

Inhibits DNA-dependent RNA polymerase F

1- Aminoglycosides  
2- Cephalosporins  
3- Glycopeptides  
4- Rifamycins  
5- Macrolides  
6- Fluoroquinolones  

PREFERRED RESPONSE: 4- Rifamycins

**Question 34 of 100**

Inhibits DNA gyrase

1- Aminoglycosides  
2- Cephalosporins  
3- Glycopeptides  
4- Rifamycins  
5- Macrolides  
6- Fluoroquinolones  

PREFERRED RESPONSE: 6- Fluoroquinolones

**DISCUSSION**

Cephalosporins and penicillin are bactericidal beta-lactam antibiotics. The mechanism of their action is inhibition of cell-wall synthesis via inhibition of peptidoglycan synthesis. Aminoglycosides irreversibly bind the 30S ribosomal proteins, inhibiting translation. Glycopeptides such as vancomycin inhibit cell-wall synthesis by disrupting the addition of cell-wall subunits. Rifamycins inhibit DNA-dependent RNA polymerase and display excellent biofilm penetration. Bacteria develop rapid resistance to Rifampin when used as monotherapy. Fluoroquinolones such as ciprofloxacin inhibit DNA gyrase. Macrolides such as erythromycin bind the 50S ribosomal subunits.
Question 35 of 100

A 14-year-old boy has failed physical therapy management for Scheuermann kyphosis, and an extension thoracolumbosacral orthosis brace is recommended. The boy and his parents are told that the brace will force his thoracic spine into normal sagittal alignment and put the anterior vertebral bodies of the thoracic segment into tension, which will induce bone growth and normalization of wedge-shaped vertebrae. What name is associated with this process?

1- Hooke's law
2- Kirchhoff's law
3- Wolff's law
4- Heuter-Volkmann principle

PREFERRED RESPONSE: 4- Heuter-Volkmann principle

DISCUSSION

The Heuter-Volkmann principle shows that bone placed in longitudinal tension will tend to stimulate longitudinal growth, and that compressive longitudinal forces inhibit longitudinal growth, making this response the best choice. Hooke's law relates to stress being proportional to strain and is not directly related to bone growth. Kirchhoff's laws apply to electrical circuit design. Wolff's law states that bone remodels in response to mechanical stress, with the correlate that increased stress causes increased growth, and decreased stress leads to bone loss.
A tendon repair is thought to be weakest during which phase of tendon healing?

1- Inflammatory
2- Proliferation
3- Maturation
4- Remodeling

PREFERRED RESPONSE: 1- Inflammatory

DISCUSSION

Healing after a tendon repair or rupture has the following stages: inflammatory, cellular proliferation, and remodeling. During the inflammatory phase, neutrophils and macrophages migrate into the injury site and release chemotactic factors that recruit fibroblasts. A tendon is thought to be weakest 5 to 21 days after repair, which coincides with the inflammatory phase. During the proliferative phase, inflammatory cells secrete cytokines and growth factors (platelet-derived growth factor, insulin-like growth factor, bone morphogenetic protein (BMP)-12 and BMP 13, and transforming growth factor-beta) that promote differentiation of fibroblasts. Fibrosis and decreased cellularity are the hallmarks of the remodeling stage.
Question 37 of 100

A 4-year-old boy has bilateral genu varum and is in the fifth percentile for height for his age. A younger sister has less severe genu varum. Radiographs reveal physeal cupping and widening on both the distal femur and proximal tibia. Laboratory studies show sodium 145 mEq/L (reference range, 136-142 mEq/L), potassium 4.0 mEq/L (reference range, 3.5-5.0 mEq/L), calcium 9.0 mg/dL (reference range, 8.2-10.2 mg/dL), phosphorous 2 mg/dL (reference range, 4-6.5 mg/dL), vitamin D 50 ng/mL (reference range, 30-100 ng/mL), and urine phosphorus 2 g/24-hour collection (reference range, 0.4-1.3 g). What effect would treatment with only Calcitriol (1,25 dihydroxy vitamin D3) have?

1- Restore normal limb alignment
2- Restore normal limb alignment and height
3- Have no effect on limb alignment and height
4- Stabilize degree of genu varum, but not improve limb alignment

PREFERRED RESPONSE: 3- Have no effect on limb alignment and height

DISCUSSION

This patient has familial hypophosphatemic rickets, a vitamin D-resistant form of rickets that is an X-linked inherited disorder. Patients are short (< 10th percentile). Varus occurs both in the distal femur and proximal tibia. Patients have increased urinary excretion of phosphorus, leading to hypophosphatemia. Calcium levels are within defined limits and vitamin D levels can be normal as well. Treatment should include phosphate and 1,25 dihydroxy vitamin D3 (calcitriol). Phosphate administration increases the plasma concentration, which lowers plasma ionized calcium concentration and further reduces plasma calcitriol concentration (removal of hypophosphatemic stimulus). Secondary hyperparathyroidism results because of both hypocalcemia and removal of the normal inhibitory effect of calcitriol on parathyroid hormone (PTH) synthesis. Elevated PTH levels will increase urinary phosphate excretion, defeating the aim of oral therapy. Addition of calcitriol is necessary to increase the intestinal absorption of calcium and phosphate to prevent secondary hyperparathyroidism. Massive doses of vitamin D alone can restore normal radiographic appearances to the epiphyses, but normal growth is not restored unless phosphate replacement is adequate.
A 35-year-old woman began to train for a half marathon. After 8 weeks of increasing her mileage, what changes can you expect in her Achilles tendon?

1- Net decrease of type I collagen
2- Net increase of type I collagen
3- Increased diameter of collagen fibrils
4- Increased cross-sectional area of the tendon

PREFERRED RESPONSE: 2- Net increase of type I collagen

DISCUSSION

Training increases turnover of type I collagen, promoting both synthesis and degradation of collagen and a net increase synthesis of type I collagen in tendon-related tissue. Strenuous endurance training has resulted in decreased collagen cross-links, suggesting increased collagen turnover, but decreased collagen maturation. In human studies, physical training results in increased turnover of collagen. Synthesis and degradation are elevated initially when beginning an exercise program, but degradation products decrease overall. It is not known if activity levels in humans affect the diameter of collagen fibrils or the cross-sectional area of tendons.
Tendon fibroblasts detect applied strain through what mechanism?

1- Induced apoptosis from tendon loading
2- Induced cell elongation from tendon loading
3- Tendon loading-mediated cell pressurization
4- Deflection of cell-cilia from tendon loading

PREFERRED RESPONSE: 4- Deflection of cell-cilia from tendon loading

DISCUSSION

The primary cilium is a cellular extension present in nearly every cell of the body, and has been shown to have critical importance in numerous functions. Emerging evidence in tendon mechanobiology suggests that mechanotransduction signaling is also mediated by the deflection of the primary cilium in response to tendon loading. "Induced apoptosis from tendon loading" would infer that each time a tendon was loaded and a portion of the tenocytes apoptosed, there would be fewer cells left, and no hope for a hypertrophy response to the loads applied. Tendon loading-mediated cell pressurization and cell elongation were previously suggested as possible means for a mechanism to mediate mechanotransduction.
Question 40 of 100

What antibiotic is recommended for an adult with Lyme arthritis of the knee?

1- Amoxicillin
2- Bactrim
3- Vancomycin
4- Tetracycline

PREFERRED RESPONSE: 1- Amoxicillin

DISCUSSION

In general, Lyme arthritis can be treated effectively with oral antibiotics. Adults can be treated with amoxicillin, doxycycline, or cefuroxime for 4 weeks. Intravenous (IV) ceftriaxone is recommended for patients with Lyme arthritis with neurologic involvement such as facial nerve palsy or meningitis, although most recent data suggest that oral antibiotics can be just as effective. For children with neurologic involvement, IV ceftriaxone or penicillin G are recommended. For antibiotic-refractory cases with persistent synovitis, arthroscopic synovectomy may be indicated.
Question 41 of 100

What mechanism is most likely responsible for the initiation of mechanical failure seen at the midstem modular junction of modular revision hip stems?

1- Fretting fatigue
2- Etching
3- Crevice corrosion
4- Abrasive wear

PREFERRED RESPONSE: 1- Fretting fatigue

DISCUSSION

The junction fracture is initiated in a fretting-fatigue mechanism and completed by a bending moment. Fretting fatigue occurs when contacting components experience cyclic loads while small oscillatory motion occurs between them. This increases tensile and shear stress, leading to small flaws that result in crack propagation. In the referenced study no evidence of corrosion was seen because there was no etching, pitting, corrosion products, or chloride formation. Etching is a finding seen in corrosion. Abrasive wear occurs when a rough surface glides against a softer surface. It is generally seen in polyethylene wear from bone or cement in third-body wear. Risk factors for stem breakage include high body mass index and lack of proximal bone support at the modular stem-junction area.
**Question 42 of 100**

Which graph best demonstrates the structural properties of the bone-ligament-bone complex of the medial collateral ligament?

1- Figure 42a  
2- Figure 42b  
3- Figure 42c  
4- Figure 42d

**PREFERRED RESPONSE: 2- Figure 42b**

**DISCUSSION**

Uniaxial tensile testing yields information about the structural properties of the bone-ligament-bone complex via the load-elongation curve (Figure 42b). The nonlinear curve shows a toe region, a linear region (slope is stiffness of femur/medial collateral ligament/tibia complex), and a failure region. The stress-strain curve (Figure 42d) demonstrates the mechanical properties of the ligament substance. A nonlinear stress-strain relationship is also seen with toe, linear, and failure regions similar to the load elongation curve. The modulus of elasticity (slope of stress/strain), tensile strength, ultimate strain, and strain energy density can be determined. The last 2 curves (Figure 42a and Figure 42c) are typical of viscoelastic materials, showing the relationship between stress/strain is not constant and depends on time of displacement or load. Figure 42a shows that stress will be reduced or "relaxed" under constant deformation. Figure 42c shows increasing deformation under constant load.
Question 43 of 100

A 45-year-old man develops a nonunion after undergoing external fixation of an open femoral shaft fracture. The procedure is revised with an open reduction and internal fixation, all intraoperative cultures are negative, and specimens from the fracture site are sent for biopsy. Histological analysis most likely will reveal

1- positive gram stain and polymorphonuclear cells that are too numerous to count.
2- bland-appearing cartilage callus.
3- Haversian remodeling.
4- lamellar bone.

PREFERRED RESPONSE: 2- bland-appearing cartilage callus.

DISCUSSION

This patient has a nonunion and intraoperative cultures that are negative. The external fixation technique would be expected to heal the fracture through an endochondral mechanism. Bland-appearing cartilage callus fits with the nonunion and with the expectation for cartilage present in the tissues taken from the failed endochondral healing site. Positive gram stains and polymorphonuclear cells that are too numerous to count suggest an active infection. Haversian remodeling and lamellar bone would be expected to be seen in fully healed and remodeling bone.
Question 44 of 100

Tendons should have what ratio of matrix protein?

1- 65% collagen type I and 35% proteoglycans
2- 80% collagen type I and 20% collagen type VI
3- 95% collagen type I and less than 5% collagen type III
4- 95% proteoglycans and 5% tenascin

PREFERRED RESPONSE: 3- 95% collagen type I and less than 5% collagen type III

DISCUSSION

Tendons consist of mainly type I collagen (95%); a small amount of collagen types III, V, VI; and proteoglycans (< 5%). Proteoglycans have highly charged glycosaminoglycan side chains that attract water and help keep tendons well hydrated. Decorin is the most common proteoglycan in tendons and has been shown to bind to collagen. Tenascin-C is a glycoprotein upregulated in tendinopathy.
In articular cartilage, Interleukin 1 (IL-1) increases

1- matrix metalloproteinase.
2- proteoglycan synthesis.
3- collagen production.
4- nitric oxide synthetase.

PREFERRED RESPONSE: 1- matrix metalloproteinase.

DISCUSSION

IL-1 stimulates matrix metalloproteinase that directly degrade cartilage. It also stimulates enzymes such as cyclooxygenase 2 and nitric oxide synthetase, which further cause tissue catabolism and damage. Glucosamine has anabolic effects on proteoglycan synthesis and can also prevent tissue catabolism by preventing an IL-1 beta-induced decrease in proteoglycan synthesis. Transforming growth factor beta has chondroprotective functions and has been shown to increase both collagen and proteoglycan synthesis while inhibiting matrix degradation and cell proliferation. Insulin-like growth factor 1 (IGF1) is produced by articular chondrocytes and increased collagen and proteoglycan synthesis. It has a role in the development of osteoarthritis. Decreased expression of IGF1 and increased binding proteins decrease the availability of the growth factors, accelerating tissue catabolism in arthritic cartilage.
Question 46 of 100

Figures 46a through 46c are the radiograph, MRI scan, and biopsy specimen of a 42-year-old patient who has a slowly enlarging thigh mass. There is no significant past medical history or history of trauma. Examination reveals a firm mass with slight tenderness. The erythrocyte sedimentation rate and complete blood count findings are within defined limits. What is the most appropriate treatment?

1- Chemotherapy, radiation, and wide resection
2- Chemotherapy and wide resection
3- Wide resection
4- Curettage

PREFERRED RESPONSE: 3- Wide resection

DISCUSSION

Parosteal osteosarcoma is a rare subtype that accounts for approximately 5% of osteosarcoma. Patients in their third and fourth decade of life are most commonly affected. The patient typically has a slow-growing mass with mild or no pain. Parosteal osteosarcoma is most often low-grade and has a relatively good prognosis compared to high-grade osteosarcoma. Wide resection is the preferred treatment and there is normally no role for chemotherapy unless the tumor dedifferentiates into a high-grade sarcoma. Curettage is reserved for benign bone tumor and should not be performed for parosteal osteosarcoma because of a high incidence of recurrence.
The initiating cellular event in development of posttraumatic osteoarthritis is attributed to which of the following?

1- Chondrocyte aging as the result of matrix degradation
2- Chondrocyte death from apoptosis
3- Cysteine protease-inhibited chondrocyte destruction
4- Interleukin-2-mediated chondrocyte hypertrophy

PREFERRED RESPONSE: 2- Chondrocyte death from apoptosis

DISCUSSION

A relatively large percentage of patients sustaining intra-articular fractures develop posttraumatic arthritis despite surgical restoration of joint incongruity and alignment. Fracture-related chondrocyte death (apoptosis) concentrated along matrix cracks in the superficial layer of cartilage has been linked to the pathogenesis of posttraumatic osteoarthritis. Apoptosis is accentuated by a series of aspartate-specific cysteine proteases. Inhibition of this cascade is a target of emerging pharmacological treatment options.
Question 48 of 100

What polyethylene processing step results in increased polyethylene wear and subsequent osteolysis?

1- Gamma irradiation in air  
2- Remelting after gamma irradiation in nitrogen  
3- Heat annealing  
4- Ethylene oxide sterilization

PREFERRED RESPONSE: 1- Gamma irradiation in air

DISCUSSION

Gamma irradiation in air is expected to result in oxidized polyethylene, which wears poorly and is expected to result in osteolysis. Many techniques have been used to reduce polyethylene wear and subsequent osteolysis. Cross-linking and thermal stabilization are 2 important techniques. Remelting and annealing are thermal stabilization methods intended to reduce the number of free radicals that are present as a result of the cross-linking process. Both remelting and heat annealing have been shown to reduce wear and osteolysis. Ethylene oxide sterilization should have no effect on the wear properties of polyethylene and should not affect its potential to contribute to osteolysis.
Question 49 of 100

The ability of compressed cortical bone to resist greater applied force in the longitudinal plane than in the transverse plane is an illustration of what material property?

1- Yield strength
2- Elastic modulus
3- Viscoelasticity
4- Anisotropy

PREFERRED RESPONSE: 4- Anisotropy

DISCUSSION

Material properties characterize mechanical functional limits of a material independent of the size or shape of that material. Anisotropic materials are those for which properties behave differently dependent on the direction of applied force. Yield strength is the load at which permanent plastic deformation begins to occur. Elastic modulus is the mathematical description of the tendency of a material to be deformed elastically in response to an applied force. The elastic modulus of a material is defined as the slope of its stress-strain curve in the elastic deformation region. Viscoelastic materials such as bone exhibit time-rate-dependent stress-strain behavior as a function of internal friction. The modulus of viscoelastic materials increase as the strain rate increases.
Question 50 of 100

Decreased sun exposure leads to decreased bone health via what mechanism?

1- Impaired ability of the liver to hydroxylate cholecalciferol
2- Impaired ability of the kidneys to hydroxylate cholecalciferol
3- Impaired parathyroid hormone (PTH) production by the parathyroid glands
4- Impaired absorption of calcium by the gastrointestinal (GI) tract

PREFERRED RESPONSE: 4- Impaired absorption of calcium by the gastrointestinal (GI) tract

DISCUSSION

Ultraviolet light from the sun is needed for skin cells to transform 7-dehydrocholesterol into cholecalciferol (vitamin D3). Once in the cholecalciferol form, it will then go to the liver and get hydroxylated into 25-hydroxyvitamin D and then to the kidneys to become 1,25-dihydroxyvitamin D. Lack of sunlight does not influence the ability of the liver or kidneys to perform hydroxylation, but it does affect the ability of the skin to create cholecalciferol, which in turn means no 1,25-vitamin D. Lack of 1,25 vitamin D has a direct impact on the GI tract’s ability to absorb calcium because the GI tract is an end organ affected by active vitamin D. The absence of 1,25 vitamin D would lead to increased levels of PTH, not decreased production of PTH.
Question 51 of 100

What proteinaceous compound binds to hyaluronic acid to function as an effective boundary molecular layer in articular cartilage?

1- Lubricin
2- Vitronectin
3- Aggrecan
4- Chondroitin sulfate

PREFERRED RESPONSE: 1- Lubricin

DISCUSSION

Hyaluronic acid (HA) is abundant in cartilage and synovial fluid and is thought to be integral to joint lubrication, although its role is not clearly understood. HA binds to lubricin, a glycoprotein, creating a cross-linked network. Boundary lubrication occurs when the fluid film has been depleted and the contacting bearing surfaces are separated only by a boundary lubricant of molecular thickness, which prevents excessive bearing friction and wear. In articular cartilage, this monolayer of glycoprotein is adsorbed on each of the opposing articular surfaces. Friction experiments in a porcine model have shown that with compression, HA diffuses out of the cartilage and becomes physically trapped and constricted by the collagen network at the interface. This in effect creates a "boundary lubricant." Vitronectin is a glycoprotein similar in the N and C terminal to lubricin. It does not bind to HA. Aggrecan is the second-most-common protein by dry weight of cartilage extracellular matrix. Aggrecan interacts with HA and link proteins to create a proteoglycan aggregate that attracts water to cartilage and gives the tissue its viscoelastic properties. Chondroitin sulfate contributes to matrix proteoglycan structure rather than boundary lubrication.
Question 52 of 100

Reverse total shoulder arthroplasty improves kinematics in the rotator cuff deficient joint by what directional change to the center of rotation?

1- Medial  
2- Lateral  
3- Posterior  
4- Proximal

PREFERRED RESPONSE: 1- Medial

DISCUSSION

Surgical indications for reverse total shoulder arthroplasty are expanding. In the setting of rotator cuff tear arthroplasty in which the native humeral head migrates superiorly, these implants impart several kinematic advantages. Implant center of rotation medial to the former joint surface improves glenoid component stability as the resultant force vector passes through the component throughout the arc of motion. A stable and fixed fulcrum for elevation is provided by matched radius of curvature between the glenoid and humeral components. A more distal center of rotation increases resting length and tone of the deltoid muscle, improving its effectiveness as a shoulder elevator. Medialized joint center of rotation increases the moment arm of the deltoid, requiring less muscle force to produce a given torque. This results in decreased articular shear stress.
Question 53 of 100

What method of spinal fixation requires the largest force to disrupt the bone-implant interface?

1- Sublaminar cables
2- Laminar hooks
3- Pedicle hooks
4- Pedicle screws

PREFERRED RESPONSE: 4- Pedicle screws

DISCUSSION

Pedicle screws have been established to produce a superior bone-implant interface in the nonosteoporotic spine according to numerous studies, but, interestingly, clinical outcomes using the varied implants have not been different.
Question 54 of 100

Amphotericin exerts antifungal activity by

1- inhibiting DNA-dependent RNA polymerase.
2- blocking folic acid synthesis.
3- binding to sterols and disrupting the cell membrane.
4- binding to cellular ribosomes and inhibiting protein synthesis.

PREFERRED RESPONSE: 3- binding to sterols and disrupting the cell membrane.

DISCUSSION

Antifungals such as amphotericin and nystatin bind to sterols in the cell membrane and disrupt its integrity, allowing diffusion of macromolecules and causing cell death. Sulfonamides and trimethopim mimic the metabolite substrate and block synthesis of metabolites such as folic acid. Rifampin inhibits bacterial RNA polymerase, blocking synthesis of RNA. Tetracycline, chloramphenicol, and clindamycin bind to ribosomes and block bacterial growth by inhibiting protein synthesis.
Question 55 of 100

What percentage of patients with metal-on-metal hip resurfacings has asymptomatic pseudotumors?

1- 5%
2- 10%
3- 20%
4- 40%

PREFERRED RESPONSE: 1- 5%

DISCUSSION

Based on a study performed by Kwon and associates in 2010, the incidence of asymptomatic pseudotumors in metal-on-metal implants was approximately 5%. The study used MRI scans and ultrasound to assess the presence of pseudotumors.
**Question 56 of 100**

What factor induces myofibrillar muscle protein synthesis (MPS)?

1. Aerobic exercise
2. Anabolic hormones (growth hormone/testosterone)
3. Resistance exercise above 60% 1-repetition maximum (RM)
4. High-repetition exercise at mid intensity (30% 1-RM)

**PREFERRED RESPONSE:** 3- Resistance exercise above 60% 1-repetition maximum (RM)

**DISCUSSION**

Resistance exercise induces myofibrillar MPS that drives muscle hypertrophy. Growth hormone/testosterone does not influence MPS in acute response to exercise or adaptive response of muscle hypertrophy to resistance exercise. Recombinant growth hormone administration does not affect MPS. Anabolic steroids do not drive adaptation in humans; an intrinsic autocrine/paracrine factor and mechanotransduction process is involved. Exercise above 60% 1-RM represents anabolic ceiling. There is a sigmoidal dose response to resistance exercise, maximum MPS occurs at > 60% 1-RM. Aerobic-zone exercise does not result in hypertrophy of skeletal muscle, but it does increase oxidative capacity.
**Question 57 of 100**

Etanercept modifies the natural history of inflammatory arthropathies through what mechanism?

1- Antagonism of the Interleukin-1 (IL-1) receptor
2- Suppression of prostaglandin production through selective inhibition of cyclooxygenase (COX)-2
3- Selective costimulation modulator inhibition of T lymphocyte activation
4- Inhibitory binding to tumor necrosis factor alpha (TNF-α)

PREFERRED RESPONSE: 4- Inhibitory binding to tumor necrosis factor alpha (TNF-α)

**DISCUSSION**

TNFα has been implicated in the pathogenesis of many chronic inflammatory diseases. Selective blockade with agents such as etanercept decreases the activation of mesenchymal cells, thereby reducing pannus formation, cartilage destruction, and osteoclastic bone resorption. IL-1 production in response to inflammatory stimulus contributes to the rapid loss of proteoglycans, leading to cartilage destruction and osteoclastic bone resorption. Recombinant forms of IL-1 antagonists such as the drug anakinra effectively block IL-1 by competitively binding to the IL-1 type I receptor. Nonsteroidal anti-inflammatory drugs inhibit the enzymes COX-1 and COX-2, which are necessary for the production of prostaglandins. Abatacept is a selective costimulation modulator that inhibits T lymphocyte activation implicated in pathogenesis of juvenile idiopathic arthritis. Methotrexate is an effective agent in the treatment of rheumatoid arthritis. The mechanism of action of this drug has not been fully elucidated. Proposed actions include decreasing cytokine production through promotion of adenosine release and inhibition of transmethylation reactions that otherwise result in accumulation of toxic compounds (spermine and spermidine).
A 62-year-old man developed a pelvic mass 5 years after undergoing a metal-on-metal hip resurfacing arthroplasty (MOMHRA). A biopsy was performed and the histologic diagnosis of pseudotumor was made. What mechanism is associated with MOMHRA-related pseudotumors?

1. Femoral head scratching from third-body debris
2. Edge loading and associated loss of fluid-film lubrication
3. Increased macrophage reactivity to *Propionibacterium acnes* (*P. acnes*)
4. Increased lymphocyte reactivity to nickel ion

PREFERRED RESPONSE: 2. Edge loading and associated loss of fluid-film lubrication

DISCUSSION

Several reports have documented the development of pseudotumors in patients undergoing MOMHRA. The incidence of pseudotumor is likely lower than 1% in this group of patients. Patients usually are asymptomatic. Recent investigation suggests that pseudotumors occur more often with increased wear attributable to edge loading. Edge loading most commonly results from abnormal contact stresses that occur in the setting of a malpositioned cup orientation. Lymphocyte reactivity to cobalt, chromium, and nickel did not significantly differ in patients with pseudotumors compared to patients without pseudotumors. Macrophage reactivity to *P. acnes* would be present in the setting of infection, but not present in the development of pseudotumors.
Alveolar rhabdomyosarcoma (ARMS) was diagnosed in a 6-year-old boy after an incisional biopsy. What is the most common genetic abnormality in this tumor?

1- EWS-Fli1 fusion gene
2- PAX3-FKHR fusion gene
3- P53 mutation
4- Retinoblastoma gene mutation

PREFERRED RESPONSE: 2- PAX3-FKHR fusion gene

DISCUSSION

ARMS is postulated to derive from precursor cells within the skeletal muscle. The embryonic derivation of these tumors is presumed to be mesoderm, the same as that of skeletal muscle. This disease occurs most commonly in young children and adolescents. In ARMS, the t(1;13) and t(2;13) translocations yield the PAX3-FKHR and PAX7-FKHR fusion genes, respectively. The t(11;22) translocation resulting in the EWS-Fli1 fusion protein is commonly found in Ewing sarcoma. P53 and retinoblastoma gene mutations predispose patients to development of osteosarcoma.
The monoclonal antibody used to treat osteoporosis (denosumab) works through inhibition of

1- receptor activator of nuclear factor kappa beta (RANK).
2- RANK ligand (RANKL).
3- osteoprotegrin (OPG).
4- tumor necrosis factor (TNF).

PREFERRED RESPONSE: 2- RANK ligand (RANKL).

DISCUSSION

Denosumab is a monoclonal antibody that targets and inhibits RANKL binding to the RANK receptor, which is found on osteoclasts. As a result, it inhibits activation of osteoclast cells and slows the process of bone resorption and bone turnover via osteoclast inhibition. The end result is similar to bisphosphonates in terms of effector cell, but the mechanism of action is very different. RANKL binds to RANK, but OPG inhibits RANK binding to RANKL. TNF is an inflammatory cytokine, and monoclonal antibodies to TNF are used to treat systemic inflammatory disease such as rheumatoid arthritis.
An article in a leading orthopaedic journal describes a randomized controlled study comparing 2 popular and comparable surgical methods for fixation of hip fractures. Patients were randomized by a predetermined computer-generated list. There was approximately 20% crossover between treatment groups. Evaluation of study outcomes (clinical and radiographs) was performed by one of the surgeons participating in the study. Enrollment goals for appropriate power were achieved and final 1-year follow-up was obtained for 65% of patients. According to Oxford Group criteria, what is the appropriate level of evidence for this study?

1- Level I
2- Level II
3- Level III
4- Level IV

PREFERRED RESPONSE: 2- Level II

DISCUSSION

Although this is a randomized controlled study, there is substantial crossover between the treatment groups, evaluation could not be blinded (radiographs) and was performed by one of the surgeons, and follow-up was moderate. According to Oxford Group criteria, this would be a Level II study.
A patient has knee pain for several days. Upon examination, he has a warm knee with a moderate effusion. Laboratory draw reveals white blood cell count (WBC) of 4000/µL (reference range, 4500-11000/µL) and a blood glucose of 80 mg/dL (reference range, 70-110 mg/dL). A knee aspiration is performed with analysis of the synovial fluid. Match the synovial fluid analysis description below with the diagnosis above.

Question 62 of 100

WBC 1300 cells/l, 20% polymorphonuclear (PMN), 2 g/dL protein, 75 mg/dL glucose, no crystals

1- Gout
2- Osteoarthritis
3- Septic arthritis
4- Hemorrhagic effusion

PREFERRED RESPONSE: 2- Osteoarthritis

Question 63 of 100

WBC 95000 cells/l, 85% PMN, 3 g/dL protein, 20 mg/dL glucose, no crystals

1- Gout
2- Osteoarthritis
3- Septic arthritis
4- Hemorrhagic effusion

PREFERRED RESPONSE: 3- Septic arthritis

Question 64 of 100

WBC 80000 cells/l, 50% PMN, 3 g/dL protein, 50 mg/dL glucose, needle-shaped birefringent crystals

1- Gout
2- Osteoarthritis
3- Septic arthritis
4- Hemorrhagic effusion

PREFERRED RESPONSE: 1- Gout

Question 65 of 100
WBC 500 cells/l, 50% PMN, 5 g/dL protein, 75 mg/dL glucose, no crystals

1- Gout
2- Osteoarthritis
3- Septic arthritis
4- Hemorrhagic effusion

PREFERRED RESPONSE: 4- Hemorrhagic effusion

DISCUSSION

Joint fluid volume should be lower than 3.5 mL with WBC < 200 cells/µl, < 25% PMN, total protein 1 g to 2 g/dL, and glucose nearly equal to that of blood. In patients who have 2000 to 100000 WBC, an inflammatory process is present such as arthritis and gout. PMN will often be < 50%, total protein slightly elevated at 3 to 5 g/dL, and glucose > 25 but less than that of blood. Presence of crystals further defines the inflammatory process of osteoarthritis vs gout. Monosodium urate gout appears in the morphology of needle-shaped crystals that are negatively birefringent under polarized microscopy. Trauma may cause a hemorrhagic effusion that is characterized with a bloody aspiration with WBC 200 to 2000 cells/µl, 50% to 75% PMN, increased total protein at 4g to 6 g/dL, and glucose levels nearly equal to that of blood.
Question 66 of 100

What factor most significantly contributes to increased risk for pseudotumor formation in patients with metal-on-metal implants?

1- Obesity
2- Edge loading
3- Female gender
4- Age older than 65

PREFERRED RESPONSE: 2- Edge loading

DISCUSSION

Obesity has not been directly associated with implant wear and pseudotumor formation. Patient factors that have been associated with increased pseudotumor formation are female gender and hip dysplasia. Studies have shown that edge loading, double-heat treatment of metal implants, and a low carbon content of the bearing surfaces have all been associated with an increased incidence of pseudotumor formation and increased metal wear debris formation.
Question 67 of 100

Osteoclastic bone resorption is stimulated primarily by what molecular interaction?

1- Parathyroid hormone (PTH)-osteoclasts  
2- Interleukin-6 (IL-6) and IL-8  
3- Receptor activator of nuclear factor kappa beta (RANK)-RANK ligand (RANKL)  
4- Osteoprotegrin (OPG)-RANKL  

PREFERRED RESPONSE: 3- Receptor activator of nuclear factor kappa beta (RANK)-RANK ligand (RANKL)

DISCUSSION

OPG is a receptor that competitively binds with RANKL, blocking the interaction with RANK and inhibiting osteoclastogenesis. PTH, secreted by the chief cells of the parathyroid gland, is active in calcium homeostasis independent of inflammatory arthropathies. PTH increases serum calcium indirectly by binding to osteoblasts, increasing expression of RANKL and decreasing expression of OPG. The interaction of RANKL to RANK in turn stimulates osteoclast precursors to fuse, forming osteoclasts to enhance bone resorption. The pannus of rheumatoid arthritis and monosodium urate crystals of gouty tophi have been shown to trigger release of inflammatory cytokines such as IL-6, IL-8 and tumor necrosis factor alpha. The key to osteoclastic bone resorption of inflammatory arthropathy is regulated by the interaction of RANKL, expressed in osteoblasts and activated T cells, and RANK, expressed in osteoclast progenitors and mature osteoclasts. In inflammatory arthropathy, RANKL expression is increased and OPG is reduced, resulting in increased cortical and subchondral bone.
What human bone disease would result from loss of osteoprotegrin (OPG) protein?

1- Multiple hereditary exostosis
2- Osteomalacia
3- Osteopetrosis
4- Osteoporosis

PREFERRED RESPONSE: 4- Osteoporosis

DISCUSSION

Loss of function of the OPG gene results in osteoporosis. Osteoprotegrin binds receptor activator of nuclear factor kappa beta (RANK) and inhibits its binding to RANK ligand (RANKL) on osteoclasts. An individual with this mutation would no longer have a way to block RANKL on osteoblasts from binding to RANK on osteoclasts. Osteoclasts would be constitutively activated, resulting in uncontrolled bone resorption. Several mouse models have confirmed the presence of this condition in knock-out mice. Multiple hereditary exostosis is an autosomal-dominant condition that results in osteochondroma formation. It has been linked to defects in the EXT1, EXT2, and EXT3 genes. Osteopetrosis would develop if a patient had overexpression of OPG or a carbonic anhydrase deficiency. Osteomalacia is the result of a deficiency in osteoid mineralization most commonly attributable to vitamin D deficiency.
Degradation of the extracellular matrix in cancer metastasis is associated with

1- thrombospondin.
2- vascular endothelial growth factor.
3- metalloproteinase (MMP).
4- platelet-derived growth factor.

PREFERRED RESPONSE: 3- metalloproteinase (MMP).

DISCUSSION

Cancer metastasis occurs most often in high-grade malignancies. Metastasis is a complex cascade of events including invasion, intravasation, dissemination, extravasation, and tumor-cell proliferation at the secondary site. Chemokines, growth factors, and matrix-degrading enzymes are critical components for every step in the metastatic process. MMPs are matrix-degrading enzymes that increase the permeability of the basement membrane, allowing cancer cell invasion and metastasis to occur. MMPs are classified according to substrate specificities: collagenases, gelatinases, and stromelysins. Vascular endothelial growth factors are proangiogenic proteins that increase neovascularity during tumor growth and metastasis. Thrombospondin-2 belongs to a family of proteins involved in cell-cell adhesion and interaction and is implicated in inhibition of tumor growth. Platelet-derived growth factor has been shown to promote tumor migration and prevent cell death.
Question 70 of 100

How are free radicals removed from highly cross-linked polyethylene?

1 - Low-dose irradiation
2 - High-dose irradiation
3 - Oxidation
4 - Thermal processing

PREFERRED RESPONSE: 4 - Thermal processing

DISCUSSION

Cross-linking of polyethylene improves its wear property via a series of steps including irradiation, thermal processing, and sterilization. Irradiation breaks carbon-hydrogen bonds in polyethylene and creates covalent bonds during cross-linking. Both low- and high-dose irradiation create free radicals that can interact with oxygen to weaken the polyethylene. Oxidation is the process through which oxygen is introduced into the polyethylene and possibly generates free radicals. Thermal processing of irradiated polyethylene removes these free radicals. Thermal processing is the heat treatment of cross-linked polyethylene to remove free radicals. Annealing and remelting are 2 thermal processing types, with annealing being the preferred technique because it results in better mechanical properties of polyethylene. Another strategy that can remove free radicals is to add an antioxidant such as vitamin E. Sterilization is the final step before the packaging of polyethylene implants.
Question 71 of 100

Trabecular bone is remodeled through the formation of

1- cutting cones.
2- Haversian canals.
3- Volkmann canals.
4- Howship lacunae.

PREFERRED RESPONSE: 4- Howship lacunae.

DISCUSSION

Trabecular bone is remodeled through osteoclast activation that creates a resorption pit known as a Howship lacuna. After the pit is formed, osteoclasts are replaced by osteoblasts that form new bone matrix. The cement line separates new bone formation from resorption. Cutting cones are created in cortical bone remodeling. Haversian canals carry nerves and blood vessels longitudinally in bone, while Volkmann canals connect different Haversian canals.
You have been waiting to enroll a patient into your recent institutional review board (IRB)-approved clinical research protocol. A patient is admitted who, upon initial screening, meets all inclusion criteria. However, he has late-stage dementia, and you are told by your research coordinator that this condition is an exclusionary criterion. This scenario demonstrates the need for which aspect of proper informed consent?

1- Provision of information
2- Competency
3- Understanding
4- Jurisdiction

PREFERRED RESPONSE: 2- Competency

DISCUSSION

Proper informed consent for research protocols includes the same elements as consent for invasive procedures. Jurisdiction is not one of the 5 elements, although it must be recognized that the process of obtaining proper informed consent for participation in a study protocol is mandated by the local IRB. The 5 elements of informed consent are:

1) The potential study subject must be able to act voluntarily, free of coercion and unfair persuasion. 2) There must be a provision of information through which the subject is informed of risks and anticipated benefits of the intervention. A discussion concerning available alternatives as well as the consequences of no treatment must also ensue. The explanation must be made in simple lay terms. 3) The participant must have the mental competency to comprehend the information. 4) There should be reasonable steps to ascertain that the subject understands all aspects of the discussion. 5) The subject actually makes a decision regarding participation.
Figures 73a through 73c are the MRI scans and biopsy specimen of a 37-year-old patient who has had a slowly enlarging right foot mass for 6 months. Medical and trauma histories are unremarkable. Examination reveals a firm mass with no substantial tenderness. What genetic defect most commonly is associated with this tumor?

1- p53 mutation  
2- SYT-SSX fusion gene  
3- Ring chromosome  
4- t(11,22) chromosome translocation

PREFERRED RESPONSE: 2- SYT-SSX fusion gene

DISCUSSION

Synovial sarcoma is the fourth-most-common soft-tissue sarcoma, often seen in young adults between 15 and 40 years of age. It affects males slightly more than females. Despite being called synovial sarcoma, only 10% of the tumor occurs in a major joint. It is the most common soft-tissue sarcoma of the foot. Synovial sarcoma can initially grow slowly and often is mistaken for a benign soft-tissue mass.
Molecular characterization of this tumor reveals that the t(x,18) translocation, representing the fusion of the SYT gene with either the SSX1 or SSX2 gene, is seen in the majority of these tumors. p53 mutations are among the most common genetic abnormalities in cancer but are not commonly associated with synovial sarcoma. Ring chromosomes are often associated with parosteal osteosarcoma. The t(11,22) chromosome translocation is most often associated with the Ewing family of tumors.
Figure 74a is the radiograph taken after a 54-year-old man underwent an uncomplicated metal-on-metal left total hip replacement 2 years ago. He continued to have hip pain and discomfort after undergoing surgery. Figure 74b is the MRI scan taken 2 years later. Figure 74c shows the hematoxylin and eosin (H&E) stain of the subsequent biopsy. The patient is noted to have an erythrocyte sedimentation rate (ESR) of 100 mm/h (reference range, 0-20 mm/h) and a C-reactive protein (CRP) of 20 mg/dL (reference range, 0.0-0.05 mg/dL). This patient should have surgery for debridement and receive administration of

1- radiation.
2- chemotherapy.
3- radiation and chemotherapy.
4- systemic antibiotics.

PREFERRED RESPONSE: 4- systemic antibiotics.

DISCUSSION

The radiograph shows a fairly normal-appearing metal-on-metal implant; however, the T1-weighted MRI scan with gadolinium contrast shows a large mass in close proximity to the joint, with probable continuity of the joint with the mass. The H&E stain shows an abundant number of neutrophils and other white blood cells, suggesting acute inflammation. This is an example of an infected pseudotumor. The abundant number of acute inflammatory cells on pathology, as well as the elevated ESR and CRP, are strong indicators of infection. In this patient, the large pseudotumor needs to be appropriately debrided, as one would do to treat an abscess, and the implants need to be removed, an antibiotic spacer placed, and systemic antibiotics started. Radiation and/or chemotherapy are not required.
RESPONSES FOR QUESTIONS 75 THROUGH 77

1- Stress
2- Strain
3- Creep
4- Modulus of elasticity
5- Toughness

Please match the biomechanical terms above with their appropriate definition below.

**Question 75 of 100**
This is the slope of the stress-strain curve

1- Stress
2- Strain
3- Creep
4- Modulus of elasticity
5- Toughness

PREFERRED RESPONSE: 4- Modulus of elasticity

**Question 76 of 100**
The amount of energy a material can absorb before failure

1- Stress
2- Strain
3- Creep
4- Modulus of elasticity
5- Toughness

PREFERRED RESPONSE: 5- Toughness

**Question 77 of 100**
Increased displacement over time attributable to a constant force

1- Stress
2- Strain
3- Creep
4- Modulus of elasticity
5- Toughness

PREFERRED RESPONSE: 3- Creep

**DISCUSSION**
Stress is force per cross-sectional area and is associated with SI units of N/m². Strain is the deformation of a material in response to an applied force and is defined...
mathematically as change in length/original length. Creep is an increased displacement over time attributable to the same force, such as during the initial period of polyethylene compression of total hips and methylmethacrylate in taper-designed cemented femoral stems. Modulus of elasticity is the slope of the stress-strain curve. It is a measure of an object's ability to resist deformation under an external load. Modulus of elasticity is unique to each material, and the higher the modulus, the more resistance to deformation. Toughness is the area under the stress-strain curve and is a measure of the amount of energy a material can absorb before failure.
Question 78 of 100

What molecules have been shown to promote fibrosis during muscle injury?

1- Insulin growth factor 1 (IGF-1)
2- Basic fibroblast growth factor (bFGF)
3- Transforming growth factor beta 1 (TGF-ß1)
4- Bone morphogenetic protein

PREFERRED RESPONSE: 3- Transforming growth factor beta 1 (TGF-ß1)

DISCUSSION

A muscle's response to injury can be divided into 4 phases: necrosis, inflammation, repair, and fibrosis. Necrosis involves the degeneration of the muscle fibrils and death. The inflammatory cells then phagocytose the debris and secrete cytokines that promote vascularity. Muscle regeneration does not occur until phagocytic cells remove the debris. Consequently, anti-inflammatory drugs may have negative effects on muscle healing by inhibiting macrophage-induced phagocytosis. Muscle fibrosis occurs at the same time as muscle regeneration and has been shown to involve TGF-ß1. IGF-1 and bFGF are important trophic factors in muscle regeneration. Bone morphogenetic protein has several functions including bone and cartilage regeneration.
Particulate wear debris is central to the mechanisms responsible for aseptic loosening. The severity of the biologic response to particulate polyethylene wear debris is directly proportional to particle

1- size.
2- number.
3- composition.
4- molecular weight.

PREFERRED RESPONSE: 2- number.

DISCUSSION

The biologic response to polyethylene is highly dependent on the type and quantity of particles. The response is clearly dose-dependent. Multiple cytokines are involved in the biologic response to wear particles, and tumor necrosis factor alpha seems to be among the most important. Its secretion increases during the biologic response to particulate wear debris. Research has shown that particles sized between 0.2 µm and 7-8 µm are the most stimulatory, but a direct proportional correlation does not exist with sizes outside of this range. A lack of correlation also applies to molecular weight and composition of polyethylene debris.
**Question 80 of 100**

What dominant intracellular proteins become directly phosphorylated as a result of bone morphogenetic protein (BMP) binding to its receptors?

1- Myc  
2- SMADs  
3- Beta-catenin (β-catenin)  
4- Adenylate cyclase

**PREFERRED RESPONSE: 2- SMADs**

**DISCUSSION**

BMP proteins, which are part of the larger transforming growth factor-beta superfamily, bind to serine/threonine receptors on the cell surface. This binding causes phosphorylation of SMAD proteins, which in turn forms a complex that enters the nucleus and initiates the transcription of several genes involved in osteoblastic differentiation. Adenylate cyclase is a transmembrane protein that acts intracellularly to activate the G protein pathways. Myc is a proto-oncogene that encodes for a transcription factor involved in numerous cell-activation pathways, but is not directly phosphorylated by BMP receptor. β-catenin is an intracellular molecule that plays a key role in the Wnt signaling pathway. This pathway is also involved in osteoblastic differentiation, but differs in target proteins within the cell.
Question 81 of 100

Figure 81 is the radiograph of a healthy 72-year-old man who has a 3-month history of medial knee pain. He denies any specific trauma. Until 3 months ago when the pain began, he had been an avid runner for many years. Initial treatment should be oral anti-inflammatory medication

1- alone.  
2- with food.  
3- with a proton pump inhibitor.  
4- with glucosamine hydrochloride.

PREFERRED RESPONSE: 3- with a proton pump inhibitor.

DISCUSSION

This patient has bone-on-bone end-stage arthritis that was asymptomatic until 3 months ago. Patients older than age 65 are at increased risk for adverse gastrointestinal effects when placed on nonsteroidal anti-inflammatory drugs, and they should be placed on a proton pump inhibitor prophylaxis at the same time. Use of glucosamine is controversial. Glucosamine hydrochloride has been shown in prospective studies to have no beneficial effect. However, glucosamine sulfate has been shown to have a positive effect on pain, but no effect on function.
Several techniques have been developed to improve the wear characteristics of polyethylene. What technique results in the largest reduction of free radicals?

1- Thermal stabilization through remelting
2- Thermal stabilization through annealing
3- Stabilizing the polyethylene with vitamin C
4- Gamma irradiation with 10 Mrads in nitrogen

PREFERRED RESPONSE: 1- Thermal stabilization through remelting

DISCUSSION

Free radicals, which are generated when polyethylene is exposed to ionizing radiation, are highly reactive and can be quenched by cross-linking with each other or via oxidation in the presence of oxygen. Thermal stabilization techniques are designed to minimize the number of remaining free radicals available to react with oxygen. Remelting is the most efficient method to reduce free radicals. Annealing also greatly reduces the number of free radicals, but cannot quench as many free radicals as remelting. Vitamin E has been shown to protect against oxidation by quenching free radicals; however, vitamin C has not shown the same benefit. Gamma irradiation with 10 Mrads will generate many free radicals regardless of the presence or absence of oxygen.
A 45-year-old previously healthy woman has experienced weakness and fatigability for 2 months. She states she feels best in the morning, but tires easily with exertion. If she sits and rests her strength improves, but she easily tires with each activity. When her fatigue is most severe, she has double vision. Physical examination is positive for ptosis with upward gaze after 20 seconds. When she holds her arms out straight she shows good initial strength, but rapidly decreasing strength with time. What is the pathologic cause of her muscle weakness?

1- Ig antibodies at the neuromuscular (NM) junction
2- Decreased release of acetylcholine at the NM junction
3- Decrease in myelin sheath of axonal nerves with loss of NM junction
4- Absence of dystrophin with excess calcium at sarcolemma

PREFERRED RESPONSE: 1- Ig antibodies at the neuromuscular (NM) junction

DISCUSSION

The patient has myasthenia gravis, which has its onset in middle age and causes progressive weakness because of the loss of acetylcholine receptors secondary to autoimmune antibodies at the NM junction. Rest periods allow uptake of acetylcholine and initial strength, but easy fatigability. Treatment is aimed at immunomodulation; acetyl cholinesterase inhibitors often coupled with thymectomy can control symptoms. Decreased release of acetylcholine at the NM junction is the effect of a nondepolarizing drug or toxin botulinum. Patients with muscular dystrophy lack dystrophin that acts at the sarcolemma to regulate calcium channels, and onset of this condition occurs at a younger age. The decrease in myelin indicates Charcot-Marie-Tooth disease and is often seen with long axon degeneration, such as in the feet and lower legs.
Question 84 of 100

You are studying a single continuous variable after administration of a defined treatment intervention. Your statistician informs you the data are not normally distributed. What is the best test to analyze the data?

1- Analysis of variance (ANOVA)
2- Regression analysis
3- Student t test
4- Mann-Whitney U test

PREFERRED RESPONSE: 4- Mann-Whitney U test

DISCUSSION

The Mann-Whitney U test is used when data are nonparametric, meaning either not normally distributed or variances are not equal among groups. Both the Student t test and ANOVA are used with parametric, normally distributed data. A regression analysis is a statistical model that allows for control of potentially confounding variables. It is used to assess the relationship between a dependent variable and (usually) multiple independent variables.
RESPONSES FOR QUESTIONS 85 THROUGH 89

1- Inhibition of vitamin K-dependent carboxylation
2- Inhibition of factor Xa through antithrombin binding
3- Binding of cyclooxygenase (COX)-1 and COX-2
4- Direct thrombin inhibition

Match the anticoagulation agents below with the appropriate mechanism of action listed above.

**Question 85 of 100**

Warfarin

1- Inhibition of vitamin K-dependent carboxylation
2- Inhibition of factor Xa through antithrombin binding
3- Binding of cyclooxygenase (COX)-1 and COX-2
4- Direct thrombin inhibition

PREFERRED RESPONSE: 1- Inhibition of vitamin K-dependent carboxylation

**Question 86 of 100**

Enoxaparin

1- Inhibition of vitamin K-dependent carboxylation
2- Inhibition of factor Xa through antithrombin binding
3- Binding of cyclooxygenase (COX)-1 and COX-2
4- Direct thrombin inhibition

PREFERRED RESPONSE: 2- Inhibition of factor Xa through antithrombin binding

**Question 87 of 100**

Fondaparinux

1- Inhibition of vitamin K-dependent carboxylation
2- Inhibition of factor Xa through antithrombin binding
3- Binding of cyclooxygenase (COX)-1 and COX-2
4- Direct thrombin inhibition

PREFERRED RESPONSE: 2- Inhibition of factor Xa through antithrombin binding

**Question 88 of 100**

Aspirin

1- Inhibition of vitamin K-dependent carboxylation
2- Inhibition of factor Xa through antithrombin binding
3- Binding of cyclooxygenase (COX)-1 and COX-2
4- Direct thrombin inhibition

PREFERRED RESPONSE: 3- Binding of cyclooxygenase (COX)-1 and COX-2

Question 89 of 100

Argatroban

1- Inhibition of vitamin K-dependent carboxylation
2- Inhibition of factor Xa through antithrombin binding
3- Binding of cyclooxygenase (COX)-1 and COX-2
4- Direct thrombin inhibition

PREFERRED RESPONSE: 4- Direct thrombin inhibition

DISCUSSION

Unfractionated heparins and the low-molecular-weight heparins bind to antithrombin, which increases the ability of antithrombin to inhibit thrombin and Factor Xa. The anticoagulant effect of warfarin is achieved by interfering with the cyclic interconversion of vitamin K and its 2, 3 epoxide, leading to hepatic synthesis of factors II, VII, IX, and X with reduced activity. Fondaparinux is a synthetic pentasaccharide that directly binds to the heparin binding site of antithrombin, inducing a conformational change in antithrombin that enhances its ability to inhibit Factor Xa. Fondaparinux is too short to bridge antithrombin to thrombin and consequently has no effect on thrombin. Aspirin irreversibly binds COX-1 and COX-2, suppressing thromboxane A2 and effectively preventing platelet aggregation. Argatroban is a direct thrombin inhibitor that prevents conversion of fibrinogen to fibrin.
Question 90 of 100

An otherwise healthy 50-year-old man who is a smoker undergoes a posterior spine fusion with instrumentation for spondylolisthesis. What can the patient do to minimize his risk for pseudarthrosis?

1. Increase calcium and vitamin D intake
2. Avoid all nonsteroidal anti-inflammatory drugs (NSAIDs)
3. Maintain smoking cessation
4. Engage in early physical therapy to strengthen the trunk musculature

PREFERRED RESPONSE: 3- Maintain smoking cessation

DISCUSSION

Smoking is the biggest risk factor for nonunion and should be strictly avoided. NSAIDs interfere with bone healing, but not as strongly as smoking. Early mobilization would potentially stress the construct, inducing movement that leads to nonunion. Without history of calcium and vitamin D deficiency, increasing intake would not decrease the risk of nonunion.
When making a comparison to autograft incorporation, the inflammatory process in allograft tissue anterior cruciate ligament (ACL) reconstruction occurs earlier.

1- occurs earlier.  
2- occurs later.  
3- is prolonged. 
4- is shortened.

PREFERRED RESPONSE: 3- is prolonged.

DISCUSSION

Compared to similar autograft, allograft tissue demonstrates a prolonged inflammatory response, slower rate of biological incorporation and remodeling, and a higher proportion of large-diameter collagen fibrils. Native ACL inserts into bone through a transition of 4 distinct zones: tendon, unmineralized fibrocartilage, mineralized fibrocartilage, and bone. This transition is not reproduced with tendon grafts, which instead heal with interposed fibrovascular scar at the graft-tunnel interface. The scar rapidly remodels to form perpendicular fibers resembling Sharpey fibers and, eventually, mature bone growth into the outer portion of the graft. The intra-articular portion of allograft undergoes an initial phase of necrosis followed by repopulation by host synovial cells into the acellular collagen scaffold. Revascularization and maturation complete the ligamentization of graft tissue.
A researcher decides she wants to look at the current total number of patients who have methicillin-resistant *Staphylococcus aureus* (MRSA) infections in a hospital on 1 particular day. What is the researcher measuring?

1- Correlation coefficient of MRSA  
2- Prevalence of MRSA  
3- Incidence of MRSA  
4- Relative risk of MRSA

PREFERRED RESPONSE: 2- Prevalence of MRSA

DISCUSSION

The prevalence of a disease is a measure of the number of cases of a disease at or during a specific time point or time period. In this case, the researcher wants to know the prevalence of disease on a given day. Incidence measures new cases of a disease or event per unit of time. Correlation coefficient is a measure of how 2 things correlate with one another, while relative risk is a statistical outcome that is often used in case-control or cohort studies to provide a measure of the risk of a particular disease occurring when a certain exposure has already occurred.
A 48-year-old man who is scheduled to undergo total knee replacement has an X-linked clotting disorder that leads to abnormal bleeding and recurrent, spontaneous hemarthrosis. Before undergoing surgery, he should have replacement therapy of

1- protein C and S.
2- vitamin K.
3- von Willebrand factor.
4- factor VIII.

PREFERRED RESPONSE: 4- factor VIII.

DISCUSSION

Hemophilia A is an X-linked recessive deficiency of factor VIII that can lead to significant bleeding problems including recurrent spontaneous hemarthroses that can lead to synovitis and joint destruction. von Willebrand disease is a lack of von Willebrand factor that leads to decreased platelet aggregation; more commonly patients have mucosal bleeding and not hemarthroses. Vitamin K deficiency is not hereditary; it is typically attributable to inadequate dietary intake, malabsorption, and loss of storage sites from hepatocellular disease. Protein C and S deficiencies are autosomal-dominant diseases that lead to thrombosis, not bleeding, as protein C and S shut off thrombin formation.
What is the recommended optimal timing of presurgical antibiotic administration to prevent infection in patients undergoing total joint replacement surgery?

1- Within 1 hour before incision
2- Within 2 hours before incision
3- Immediately after incision
4- Within 1 hour after incision

PREFERRED RESPONSE: 1- Within 1 hour before incision

DISCUSSION

The current recommendation for antibiotic prophylaxis for major orthopaedic surgical procedures is to administer intravenous antibiotics within 1 hour of surgical incision. Redosing of antibiotics should occur 3 to 4 hours after the initial dose for procedures that extend beyond 3 to 4 hours. Little evidence supports postsurgical antibiotic use beyond 24 hours. As you move beyond 1 hour from time of administration of antibiotics, risk for infection increases and rates of bacterial cell death decline. It is not acceptable to administer presurgical antibiotics after incision.
Question 95 of 100

Bacterial resistance to antibiotics in biofilm is an example of

1- avoidance.
2- decreased susceptibility.
3- inactivation.
4- mutation.

PREFERRED RESPONSE: 1- avoidance.

DISCUSSION

Three basic mechanisms of antibiotic resistance have been identified: avoidance, decreased susceptibility, and inactivation. Biofilm formation is a classic example of avoidance, whereby the biofilm creates a physical barrier to the antibiotic. Bacteria can decrease their susceptibility to antibiotics by mutating the antibiotic target or generating a mechanism to inactivate the antibiotic. Biofilm formation develops when a sufficient mass of bacteria forms on a surface. The cell-to-cell signaling becomes sufficient to activate transcription of genes needed for biofilm formation in a process known as quorum sensing. Once the bacteria produce a mature biofilm, they enter a greatly reduced or stationary phase of growth. Lastly, high-shear environments seem to stimulate biofilm production.
A 19-year-old man sustains a thigh contusion over his quadriceps muscle while skateboarding. He is treated with several days of immobilization followed by gradually increasing range of motion and activity. Histologic analysis of a biopsy of the healing muscle in the mobilization state at 4 weeks from the date of injury would be characterized by

1- a decreased density of nerve fibrils.
2- lymphocytes and macrophages infiltration.
3- parallel penetration of muscle fiber through scar tissue.
4- lengthening and narrowing of myotubes.

PREFERRED RESPONSE: 3- parallel penetration of muscle fiber through scar tissue.

DISCUSSION

Skeletal muscle contusions are a common cause of morbidity from sports-related injuries. The healing response involves a complex balance among muscle repair, regeneration, and scar-tissue formation. Animal models of muscle contusion have demonstrated a time-dependent histological response to postinjury protocols of immobilization and remobilization. Mobilization initiated after a brief period of immobilization resulted in better penetration of regenerative muscle through limited connective tissue scar in line with native surrounding muscle. Early mobilization in an in vivo muscle contusion model resulted in a progressive increase in myotubule, early nerve regeneration, and reduced inflammation. Immobilization results in disorganized penetration of muscle fiber through dense connective scar tissue with immobilization.
A patient with Paget disease who is intolerant of bisphosphonates is given calcitonin. What is the mechanism of action of calcitonin?

1- Promotes reabsorption of phosphate in the renal tubules
2- Interferes with osteoclast maturation
3- Interferes with intestinal absorption of calcium
4- Upregulates osteoblast formation

PREFERRED RESPONSE: 2- Interferes with osteoclast maturation

DISCUSSION

Calcitonin is a hormone that reduces serum calcium concentration by directly interfering with osteoclast maturation via receptors. Calcitonin inhibits phosphate reabsorption and decreases calcium reabsorption in the kidneys. By attenuating cartilage breakdown and stimulating cartilage formation via inhibitory pathways of matrix metalloproteinases, calcitonin also has a chondro-protective effect on articular cartilage. Calcitonin has no major effects on intestinal absorption of calcium, but may aid in small-bowel secretion of sodium, potassium, chloride, and water. Calcitonin also has no receptor effect on osteoblasts.
A cartilage water content increase is the hallmark of which osteoarthritis stage?

1- Prearthritis
2- Early
3- Late
4- Terminal

PREFERRED RESPONSE: 2- Early

DISCUSSION

The first stage of osteoarthritis is marked by an increase in water content secondary to disruption of the matrix framework. This is followed by an increase in chondrocyte anabolic and catabolic activity in response to tissue damage. Wnt-induced signal protein 1 increases chondrocyte protease expression. Failure to restore tissue balance ultimately leads to continued destruction and osteoarthritis. One hallmark of osteoarthritic cartilage is a reduced repair mechanism attributable to decreased chondrocyte response to growth factor stimulation (transforming growth factor-alpha and insulin-like growth factor-1). Mitochondrial dysfunction and increased production of reactive oxygen species may promote cell senescence, a progressive slowing of cellular activity. Microscopic evidence of cartilage degeneration begins with fibrillation of the superficial and transition zones, followed by disruption of the tidemark by subchondral blood vessels and eventual subchondral bone remodeling. This process ultimately leads to cartilage degradation with decreased water content in the late and terminal phases of osteoarthritis.
Question 99 of 100

Figures 99a through 99c are the hematoxylin and eosin (H&E) stain, S-100 stain, and MRI scan, respectively, of a tumor removed from a 42-year-old man. This type of tumor is most commonly associated with a condition that is transmitted in what type of pattern?

1- Autosomal-recessive inheritance
2- Autosomal-dominant inheritance
3- X-linked recessive inheritance
4- X-linked dominant inheritance

PREFERRED RESPONSE: 2- Autosomal-dominant inheritance

DISCUSSION

The T2-weighted MRI scan shows a large soft-tissue mass within the anterior thigh in a similar location as one would expect to find the femoral nerve. Figures 99a and 99b show H&E and S-100 staining of the mass shown in the MRI scan. The diffusely positive S-100 staining and pleomorphic large elongated spindle-shaped blue cells are characteristic of a malignant peripheral nerve sheath tumor (MPNST). MPNSTs are commonly associated with neurofibromatosis type 1 (NF1), which is inherited in an autosomal-dominant inheritance pattern. The other responses are incorrect for NF1.
Question 100 of 100

A man who weighs 75 kg (165 pounds) is scheduled for elective total hip arthroplasty. He reports a history consistent with anaphylaxis from penicillin. Within 1 hour of the incision the patient should receive 1000 mg of

1- cefazolin.
2- cefuroxime.
3- vancomycin.
4- clindamycin.

PREFERRED RESPONSE: 3- vancomycin.

DISCUSSION

The recommended antimicrobial prophylaxis for total hip arthroplasty is cefazolin or cefuroxime unless the patient has an allergy to beta-lactam antibiotics. Patients with an allergy should be given vancomycin 10 to 15 mg/kg or clindamycin 600 to 900 mg. Because this patient has an allergy to penicillin, he should be given 1000 mg of vancomycin within 1 hour of the skin incision.