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CLINICAL CASES OF PHYSIOLOGY AND PATHOPHYSIOLOGY
PART 1

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This publication contains educational and methodological materials for self-preparation for medical students of 2nd and 3rd year studying. Clinical cases and MCQs of IFOM and STEP 1 of physiology and pathophysiology provide accurate information for preparing for independent exams and understanding the theoretical materials.

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SECTION ACTION POTENTIAL
MCQs STEP 1

1. An 82-year-old woman is brought to the emergency room complaining of nausea, vomiting, muscle cramps, and generalized weakness. Laboratory analysis reveals significant hyperkalemia. Elevations of extracellular potassium ion concentration will have which of the following effects on nerve membranes?

A. The membrane potential will become more negative
B. The sodium conductance will increase
C. The potassium conductance will increase
D. The membrane will become more excitable
E. The Na+-K+ pump will become inactivated

2. A 13-year-old boy on the junior high wrestling team experiences attacks of proximal muscle weakness that last from 30 minutes to as long as 4 hours following exercise and fasting. The trainer attributed it to the symptoms of fatigue, but his mother recalled having similar symptoms when she was dieting. Genetic testing revealed an inherited channelopathy. Electrically excitable gates are normally involved in which of the following?

A. The depolarization of the end-plate membrane by acetylcholine
B. Hyperpolarization of rods by light
C. Release of calcium from ventricular muscle sarcoplasmic reticulum
D. Transport of glucose into cells by a sodium-dependent, secondary active transport system
E. Increase in nerve cell potassium conductance caused by membrane depolarization

3. Gamma-aminobutyric acid (GABA) is an amino acid that functions as a neurotransmitter in the central nervous system. GABAtypically causes increased chloride conductance and functions as an inhibitory transmitter. Assume that the equilibrium potential for chloride (ECl−) in a particular cell is −80 mV and that application of GABA inhibits the cell without any change in resting membrane potential. What is the resting membrane potential of the cell?

A. +80 mV
B. 0 mV
C. −70 mV
D. −80 mV
E. −90 mV

4. Figure 2-23 shows the change in the membrane potential of a postsynaptic neuron caused by addition, at the arrow, of a neurotransmitter. The resting membrane potential

of this cell is −80 mV. Relevant equilibrium potentials for Ca2+, Na+, Mg2+, Cl−, and K+ are, respectively, +120 mV, +60 mV, 0 mV, −80 mV, and −90 mV. This neurotransmitter likely increases the conductance of which of the following ions?

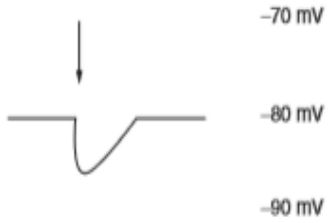


FIG. 2-23

A. Ca2+
B. Cl−
C. K+
D. Mg2+
E. Na+

5. Which of the following proteins uses the sodium electrochemical gradient to actively transport a solute into the cell?
A. calcium-ATPase
B. GLUT2
C. Na+, K+-ATPase
D. Na+: Ca2+ countertransport protein
E. SGLT-1

ANSWERS MCQs STEP 1

1. The answer is C. An increase in extracellular K+ makes the membrane potential more positive. Depolarizing the membrane opens K+ channels causing an increase in membrane conductance. Prolonged depolarization, whether caused by an increase in extracellular K+ or by an action potential, inactivates Na+ channels, which decreases the excitability of the nerve membrane. The activity of the Na+-K+ pump is reduced in hypokalemia, not hyperkalemia.

2. The answer is E. Electrically excitable gates are those that respond to a change in membrane potential. The most notable electrically excitable gates are those on the sodium and potassium channels that produce the nerve action potential. The potassium channel gate is opened by depolarization. Ventricular muscle SR releases its calcium in response to an increase in intracellular calcium. The gates opened by ACh are chemically excitable gates. In rods, sodium channels are closed when cGMP is hydrolyzed. Electrically excitable gates do not regulate the active transport of glucose.

3. The answer is D. This problem addresses two issues: (1) the mechanism of action of inhibitory neurotransmitters and (2) the relationship of equilibrium potential and membrane potential. First, an inhibitory neurotransmitter acts by increasing

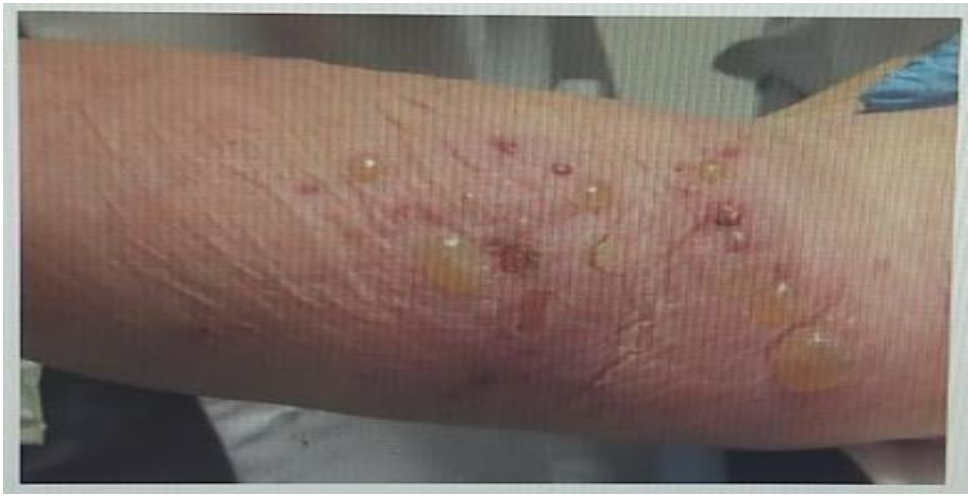
conductance of an ion the equilibrium potential of which is either equal to or more negative than the cell resting membrane potential. If the equilibrium potential of the ion is more negative than the resting membrane potential, increasing the conductance of that ion will hyperpolarize the membrane—will generate an inhibitory postsynaptic potential (IPSP). Second, if the equilibrium potential of the ion is equal to resting membrane potential, increasing the conductance of that ion will "clamp" the membrane potential more tightly at its resting level—this will make the cell less excitable. In this problem, the membrane potential must equal −80 mV (D). If, and only if, the resting membrane potential equals the equilibrium potential for an ion, will an increase in the conductance to that ion not cause a change in membrane potential.

4. The answer is C. Increase in the conductance of an ion, the equilibrium potential of which is negative with respect to the cell's resting membrane potential, will cause the membrane potential to hyperpolarize (to become more negative). Increased K+ permeability would thus cause hyperpolarization, since its equilibrium potential is negative with respect to the cell's resting membrane potential. Increased Ca2+, Na+, or Mg2+ permeability (choices A, D, and E) would cause the cell membrane potential to depolarize. Increased Cl_ permeability (choice B) would not alter the membrane's potential.

5. The answer is E. SGLT-1 is a sodium-dependent cotransport protein that uses the sodium electrochemical gradient to actively move glucose into the cell. GLUT2 (choice B) does transport glucose, but it is a facilitated diffusion carrier that moves glucose down its concentration gradient. The Na, K-ATPase (choice C) is a primary active transport protein. It uses the energy liberated from ATP hydrolysis to actively transport sodium and potassium. It establishes and maintains the sodium electrochemical gradient. The sodium:calcium countertransport protein (choice D, also termed NCX) uses the sodium electrochemical gradient to move calcium ions out of, not into, the cell. The calcium ATPase (choice A, also termed PMCA) is a primary active transport protein that actively transports calcium out of the cell. Both NCX and PMCA serve to maintain a low intracellular calcium concentration.

SECTION MUSCULOSKELETAL SYSTEM
MCQs IFOM

1. A 60-year-old man presents to the physician complaining of a “strange rash” that began with itching but has worsened over the past 2 weeks. He now has the fluid-filled blisters: shown in the image. Past medical history is significant for a similar episode 7 months ago involving his inner thighs. Physical examination reveals blisters on many areas of his skin. When slightly rubbed, the blisters do not exfoliate. Histopathologic examination of one of the lesions demonstrates immunoglobulin deposition. The physician prescribes atopical corticosteroid treatment.



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Which of the following cellular structures is most likely affected by this patient’s condition?

A.Connexons

B. Desmosomes

C. Hemidesmosomes

D. Nuclear Lamina

E. Tight junction

2. A 65-year-old man comes to the clinic because of a persistent headache, dizziness, and severe hip pain during the past year. He says that his hat no longer fits him. He also reports ringing in his ear and some hearing loss. He has a history of hypertension and diabetes mellitus controlled with lisinopril and metformin. His paternal grandfather had osteosarcoma. Temperature is 30.9° C (87.7° F), blood pressure is 126/82 mm Hg, pulse is 79/min, and respiratory rate is 16/min. Physical examination elicits bone pain. Serum calcium, parathyroid hormone, and phosphorus levels are within reference ranges. Elevation of which of the following markers is associated with this patient’s most likely cause of bone pain?

A. Alkaline phosphatase

B. Calcitonin

C. Gamma-glutamyl transferase
D. Tartrate resistant acid phosphatase
E. Urinary deoxypyridinoline

3. A 35-year-old woman comes to the clinic because of progressive weakness of the shoulders and legs for the past 3 months. She has been having difficulty combing her hair, buttoning her blouses, walking upstairs, and lifting objects. She especially has great difficulty in getting up from the seated position. She does not notice anything that improves or worsens her weakness, it does not seem to change throughout the day or with repeated efforts, and she has no pain. She does not take any medications. Her mother has systemic lupus erythematosus. Vital signs are within normal limits. Physical examination shows symmetrical weakness of the proximal muscles in the both upper and lower extremities.There are no rashes, lesions, or other remarkable findings. Which of the following is the most likely cause of this patient's condition?

A. Anti-U1 RNP (ribonucleoprotein) antibodies
B. Autoantibodies to postsynaptic ACh receptor
C. Autoantibodies to presynaptic Ca2+ channel
D. Endomysial inflammatory infiltration
E. Endoneurial inflammatory infiltration
F. Periarticular inflammation
G. Perimysial inflammatory infiltration

4. An 83-year-old man come for evaluation because of a 6-month history of weakness and increasing pain in his lower back. He denies numbness or tingling, sensory changes, fever, or chills. His history is otherwise noncontributory. Physical examination demonstrates a somewhat disheveled appearance and poor dentition with caries. His range of motion in the lumbar region is only mildly restricted due to pain, and lower extremity gross strength testing reveals 5/5 strength bilaterally for hip flexion, hip extension, knee flexion, knee exiension, dorsiflexion, and plantarflexion. Lumbar spine and pelvis are tender to palpation. Laboratory test results show:

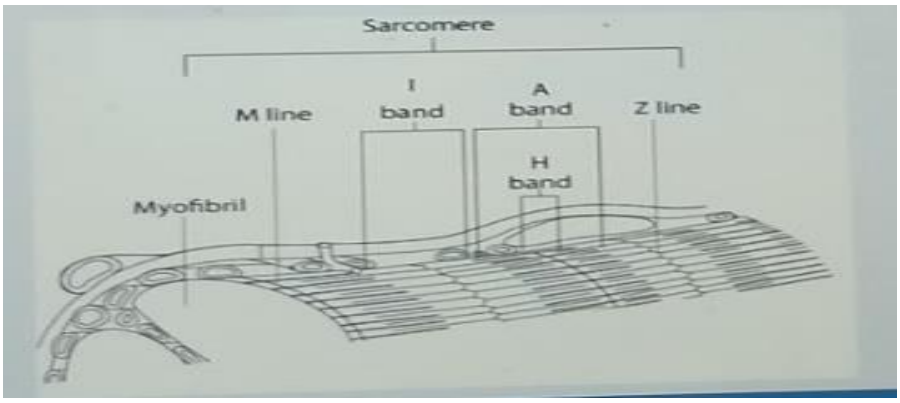
Hemoglobin: 14.1 g/dL
Hematocnt: 42 4 %
WBC: 6.7 x 103/uL
Platelets: 198 000/mm?
Sodium: 140 mEq/L
Potassium: 3.6 mEq/L
Chlonde: 105 mEq/L
CO2: 25 mEq/L
BUN:13 mg/dL
Creatinine. 0.96 mg/dL

Which of the following is the most likely underlying cause of patient's condition:

A. Bone metastasis
B. Defective collagen synthesis
C. Paget disease
D. Parathyroid carcinoma
E. Vitmin D deficiency

5. A 75-year-old man dies overnight in the intensive care unit after being there for the past 6 days. Since the cause of his illness and subsequent death is still unclear to the care team, the patient's family consents to the physician's request for an autopsy. On initiation of the autopsy the following morning, the muscles of the body are hard and very stiff, and it is difficult to move and manipulate his limbs. The inability of the muscle fibers to relax is due to specific biochemical changes within the muscle.
Which of the following mechanisms is impaired, preventing normal movement?
A. Binding of actin to myosin
B. Binding of troponin to tropomyosin
C. Power stroke of the myosin head
D. Release of actin from myosin
E.Uptake of calcium into the sarcoplasmic reticulum

6. A 63-year-old man is found unconscious by his wife and is transported to the emergency department experiencing a tonic-clonic seizure. The patient has a history of seizures since he was 20 years old, and they have been well controlled by the anticonvulsant levetiracetam, with few breakthroughs. The patient is eventually stabilized with an intramuscular injection of the sedative midazolam in the emergency department, terminating the seizures. The patient is then interviewed regarding what he remembers. He is unable to recall any events of the seizure, but complains of muscle aches. Recall that the sarcomere is the basic functional unit of skeletal muscle (illustration).



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Any shortening of muscles due to seizure would result in which of the following changes in length within each shortening sarcomere?
A. Lengthening of A band; no change in H band; shortening of I band
B. No change in A band; lengthening of H band; lengthening of I band

C. No change in A band; shortening of H band; shortening of I band
D. Shortening of A band; no change in H band; shortening of I band
E. Shortening of A band; shortening of H band; no change in I band

MCQs STEP 1

1. A 21-year-old man is competing in a weight-lifting competition. He lifts 325 lb over his head and holds it there for 5 seconds. Suddenly, his arms give way and he drops the weight to the floor. Which of the following receptors is responsible for this sudden muscle relaxation?
A. Free nerve ending
B. Golgi tendon organ
C. Merkel disk
D. Muscle spindle
E. Pacinian corpuscle

2. A 48-year-old white female secretary presents with progressive difficulty typing over the past month. She also notes that her hands begin to feel numb and weak after typing for long periods of time. On testing, which of the following deficits would be predicted?
A. Difficulty in abducting the fifth finger
B. Difficulty in adducting the thumb
C. Difficulty in flexing digits two and three at the metacarpophalangeal joints
D. Loss of sensation over the lateral half of the dorsum of the hand
E. Loss of sensation over the lateral half of the palm
F. Loss of sensation over the medial half of the dorsum of the hand
G. Loss of sensation over the medial half of the palm

3. In a controlled experiment, radiolabeled ATP is injected into an isolated muscle. The muscle is stimulated and allowed to contract for 10 seconds. An autoradiogram from a biopsy of the muscle will show radiolabeled ATP bound to
A. actin
B. myosin
C. sarcoplasmic reticulum
D. tropomyosin
E. troponin C

4. A 62-year-old male who was diagnosed with lung cancer also displays weakness in his arms and legs. A battery of tests are administered to the patient, including those involving nerve conduction. The nerve conduction test reveals a reduction in the compound motor action potential relating to muscles of the hand. However, the amplitude of this potential improves significantly following exercise involving the relevant muscles. Which of the following is the most likely diagnosis?

A. Ms
B. Als
C. Myasthenia gravis
D. Lambert-Eaton syndrome
E. Md
5. A 64-year-old male was admitted to the hospital with edema and congestive heart failure. He was found to have diastolic dysfunction characterized by inadequate filling of the heart during diastole. The decrease in ventricular filling is due to a decrease in ventricular muscle compliance. Which of the following proteins determines the normal stiffness of ventricular muscle?
A. Calmodulin
B. Troponin
C. Tropomyosin
D. Titin
E. Myosin light chain kinase
6. A 12-year-old male with muscular dystrophy is found to have a mutation of the gene that encodes the protein dystrophin. Genetic alterations in dystrophin lead to progressive muscular weakness because dystrophin provides structural support to the sarcolemma by binding which of the followinig?
A. B-dystroglycan to laminin
B. Actin to b-dystroglycan
C. Actin to the z lines
D. Z lines to m lines e
E. Z lines to the sarcolemma
7. A 65-year-old man with severe congestive heart failure (CHF) is unable to climb a flight of stairs without experiencing shortness of breath. After several years of therapy with first-line drugs for heart failure, we empirically try digoxin to improve cardiac muscle contractility. Within 4 weeks, he has a marked improvement in his symptoms. Which of the following best describes the main cellular action of digoxin that accounts for its ability to improve his overall wellness and his cardiovascular function in particular?
A. Activates β1-adrenergic receptors
B. Facilitates gtp binding to specific g proteins
C. Increases mitochondrial calcium (ca2+) release
D. Inhibits sarcolemmal na+-k+-atpase
E. Stimulates cyclic adenosine 5’-monophosphate (camp) synthesis
8. A healthy 17-year-old male tells his doctor during a normal check-up visit that “his muscles gave out” when he recently attempted to lift a heavy load. On questioning, he answers that he did not experience any other neuromuscular problems after this

experience. What is the most likely mechanism responsible for the abrupt cessation of skeletal muscle contraction?

A. Activation of alpha motor neurons

B. Activation of gamma motor neurons

C. Activation of golgi tendon organs

D. Activation of muscle spindles

E. Skeletal muscle ischemia

9. Which of the following compounds directly functions in excitation contraction coupling in smooth but not skeletal muscle?

A. Actin

B. Calcium

C. Myosin

D. Myosin light chain kinase

E. Troponin

10. A 53-year-old man is being treated for hypertension and diabetes. His medications include insulin and propranolol. He presents at his physician's office complaining of muscle weakness. Blood tests reveal hyperkalemia (elevated serum potassium) as well as elevated BUN (blood urea nitrogen). Propranolol is gradually eliminated and his insulin dosage is adjusted. His serum potassium normalizes and his muscle weakness is alleviated. What probably caused his muscle weakness?

A. High potassium-mediated block of acetylcholine receptors

B. High potassium-mediated block of skeletal muscle calcium channels

C. Motor neuron hyperpolarization

D. Skeletal muscle depolarization with resultant na-channel inactivation

E. Skeletal muscle hyperpolarization with resultant na-channel blockade

11. Which of the following statements concerning skeletal muscle is correct?

A. Active tension depends on the extent of overlap between thick and thin filaments

B. During contraction, thin filaments shorten and thick filaments maintain constant length

C. Significant passive tension is generated at normal rest fiber length

D. Tension generation depends on myosin attachment to the z line

E. Velocity of shortening is independent of fiber load

12. Lambert-Eaton myasthenic syndrome (LEMS) is an autoimmune disorder in which autoantibodies attack voltage-gated calcium channels in the presynaptic nerve terminal. Acharacteristic manifestation of LEMS is limb muscle weakness. A decrease in which of the following would you expect to see in LEMS?

A. Activation threshold for the action potential

B. Amplitude of the action potential

C. Amplitude of the miniature end-plate potential (mepp)

D. Magnitude of the end-plate potential (epp)
E. Quantal content

13. Cardioactive steroids, like digoxin, exert a positive ionotropic effect on heart muscle cells. Because of this activity, they can be used clinically to increase contraction of a failing heart. Which of the following proteins is important in the mechanism of action of digoxin on the cardiac muscle cell?

A. N-type calcium channels
B. Na+ : Ca2+ exchange protein (NCX)
C. plasma membrane calcium ATPase (PMCA)
D. potassium channels
E. sodium channels

14. Malignant hyperthermia is a relatively rare genetic disorder, found in approximately one in 10,000 individuals. Affected individuals can exhibit a life-threatening response to inhalation anesthetics, which entails elevated core body temperature, skeletal muscle rigidity, and elevated blood carbon dioxide levels. Based on these observed symptoms, which of the following is most likely present in malignant hyperthermia?

A. decreased release of acetylcholine at the neuromuscular junction
B. increased activation of myosin light chain kinase
C. increased activation of skeletal muscle potassium channels
D. increased activation of the calcium release channels of the sarcoplasmic reticulum
E. inhibition of skeletal muscle sodium channels

ANSWERS MCQs IFOM

1. The answer is C. This patient has fluid-filled blisters on many areas of his skin that do not exfoliate upon rubbing. The presence of immunoglobulins with this presentation usually suggests bullous pemphigoid (BP). The earliest blisters may appear urticarial with pruritus. BP is associated with a negative Nikolsky sign, which means the blisters do not exfoliate when rubbed. Direct immunofluorescence will show linear IgG and C3 deposition at the dermal-epidermal junction. The presentation of BP may vary between patients, but the elderly are most afflicted and report the classic bullae depicted in the image. BP is caused by an autoimmune attack against hemidesmosomes, which are junctional complexes that anchor the basal layer of the epidermis to the underlying bdsement membrane. Loss of normal hemidesmosome function leads to bullae formation because the epidermis is lifted from the dermis as a continuous sheet. BP can be self-resolving, but corticosteroids, such as prednisone, may be given to relieve itching and allow healing. Connexons are proteins that form gap junctions and are not affected in BP. Desmosomes are affected in pemphigus vulgaris, which has a positive Nikolsky sign (exfoliation of blisters when rubbed). Nuclear lamina are not involved in cell-cell adhesion, so they are unaffected in BP. Tight junctions are not involved in the formation of fluid-filled blisters.

2. The answer is A. This patient is a 65-year-old man with a history of hypertension and diabetes mellitus who has severe bone pain, headache, tinnitus, vertigo, and hearing loss. This is most suggestive of Paget disease. Paget disease of the bone is a metabolic bone disorder of abnormal bone remodeling. It affects the skull, thoracolumbar spine, pelvis and long bones of lower extremities. Bone remodeling is a normal process that involves a balance between osteoblast and osteoclast activity to maintain normal bone structure. Osteoblasts are responsible for bone formation and osteoclasts are responsible for resorption of bone. RANKL in osteoblasts will bind to RANKL receptors on osteoclasts to signal osteoclasts to resorb bone. Osteoblasts also contain osteoprotegerin (OPG), which inhibits RANKL from binding to its receptors on osteoclasts and prevents excessive bone resorption during remodeling. In Paget disease, there is increased osteoclastic activity and increased osteoblastic activity leading to lytic phase, mixed phase, and sclerotic phase of bone structure. Increased osteoclastic activity during the lytic phase leads to increased bone resorption. This is followed by a mixed phase, where resorption is met by compensatory bone formation by osteoblasts, which eventually transitions to a sclerotic phase where osteoblast function predominates. However, although osteoblasts are promoting bone formation during this phase, the matrix is woven and has less structural integrity. Nonetheless, this robust formation of bone can appear as thickening on x-ray study or present clinically as an increase in skull diameter, headaches, tinnitus, or vertigo (otosclerosis).

When evaluating for Paget disease, serum phosphate, calcium, and parathyroid hormone will be within reference ranges with an increased alkaline phosphatase (ALP) concentration. An increased ALP concentration is the result of increased osteoblastic activity, as described above. Notably, increased ALP concentrations can be seen in cholestasis, obstructive biliary diseases, osteosarcoma, or metastasis to bone (commonly from prostate cancer).

The other answer options are incorrect for the following reasons:

Gamma-glutamyltransferase (GGT) is seen in patients with increased alcohol use or with biliary or liver disease like primary sclerosing cholangitis or primary biliary cholangitis.

Deoxypyridinoline is a by-product of osteoclasts during bone resorption. Although this patient's symptoms may be mediated by bone pathology, it is not only from osteoclastic activity.

Calcitonin is released by parafollicular C cells of the thyroid glands and inhibits osteoclast activity, which leads to inhibition of bone resorption. This patient's symptoms of bone pain, hearing loss, and tinnitus are not suggestive of osteoclastic inhibition.

Fibroblast growth factors are cell signalling proteins released during tissue remodeling. This patient's symptoms are suggestive of an underlying bone remodeling process.

Tartrate-resistant acid phosphatase comes from osteoclasts. It is primarily used as a marker of hairy cell leukemia, which is characterized by fatigue, weight loss, shortness of breath, petechiae, or lymphadenopathy.

3. **The answer is D.** The patient is a 35-year-old woman with signs of proximal muscle weakness (difficulty standing from a seated position, raising arms above head, etc.). Her physical examination is significant only for weakness with no signs of a rash. Therefore, the most likely diagnosis is polymyositis.

Polymyositis is an autoimmune disorder that has progressive onset of proximal muscle weakness without pain. It is commonly associated with other autoimmune diseases. It is caused by endomysial infiltration with CD8+ T cells and is associated with overexpression of major histocompatibility complex (MHC) class |, which allows the muscle to become susceptible to destruction. Workup for polymyositis shows increased creatinine kinase enzymes and positive for antinuclear antibodies (ANA), anti-Jo-1, anti-SRP and anti-Mi-2 antibodies. Results of a muscle biopsy would show inflammation, patchy necrosis, and regeneration and fibrosis of muscle fibers. Unlike dermatomyositis, there is no cutaneous involvement. Dermatomyositis is an autoimmune disorder that also presents with proximal muscle weakness, but with classic cutaneous manifestations like Gottron papules (raised erythematous plaques over joints on hands) and a heliotrope rash of periorbital area and cheeks. Muscle

biopsy results would show perimysial infiltration and perifascicular atrophy and patchy necrosis. Both polymyositis and dermatomyositis can occur individually or as a result of paraneoplastic syndrome. Associated cancers include ovarian adenocarcinoma, ling cancer colorectal cancer, and non-Hodgkin lymphoma. First – line treatment is long-term use of corticosteroids. The other answer choices are not the best choices for the following reason:

Perimysial inflammatory infiltration occurs in patients with dermatomyositis, which is a myopathy that involves proximal muscle weakness and a malar rash, Gottron papules, or a heliotrope rash. Infiltration is with CD4+ T cells. Unlike polymyositis, there is cutaneous involvement in dermatomyositis.

Polymyalgia rheumatica is characterized by proximal muscle weakness associated with severe pain, fever, and weight loss. It is an inflammatory disorder which involves periarticular inflammation, especially of the shoulders.

Endoneurial inflammatory infiltration is a demyelinating polyneuropathy associated with ascending weakness and decreased reflexes that occurs 2-4 weeks afier a respiratory or gastrointestinal illness. This is seen in patients with Guillain-Barré syndrome.

Anti-U1 RNP antibodies are suggestive of mixed connective tissue disease (MCTD), a disorder that involves polymyositis, systemic lupus erythematosus, and systemic sclerosis. Patients may have muscle weakness, joint pain, or Raynaud's phenomenon.

Proximal muscle weakness in Lambert-Eaton myasthenic syndrome is caused by autoantibodies to presynaptic Ca2+ channel that lead to insufficient muscle contractions. Continued use of the limbs will relieve muscle weakness. Autoantibodies to postsynaptic ACh receptor describes the cause of myasthenia gravis, which presents as muscle weakness.

4. The answer is E. This older man presents to his physician with weakness and pain in his lower back and shows poor dentition. A radiograph shows lumbar fracture deformities and diffuse osteopenia, and his lab values reveal hypocalcemia and hypophosphatemia, which are concerning for osteomalacia. Osteomalacia describes the softening of bone that may result from prolonged deficiency of vitamin D, which can cause vertebral fractures and reduced bone density. Vitamin D is activated initially in the skin, and then undergoes two hydroxylations: one in the liver, and the other in the kidney, under the influence of parathyroid hormone (PTH).

Vitamin D is a fat-soluble vitamin that requires normal liver function for absorption through the small bowel. Activated vitamin D increases calcium and phosphate reabsorption in the small intestine and increases bone resorption. Therefore, in the absence of adequate vitamin D, low serum levels of calcium (hypocalcemia) and phosphate (hypophosphatemia) may result Additionally, secondary hyperparathyroidism may occur as the parathyroid glands try to increase serum calcium

levels and promote hydroxylation of vitamin D. All three of these lab abnormalities appear in this patient. The deficiency in active vitamin D can be a result of poor dietary intake, malabsorption, reduced exposure to sunlight, hepatic disease (including cirrhosis), renal failure, small-bowel disease, and pancreatic insufficiency, among others. In elderly patients, vitamin D deficiency often is secondary to poor nutrition/feeding, often caused by poor dentition, loss of appetite, or creeping dementia. The patient's exam revealed poor dentition and, given his disheveled appearance, he may also be experiencing creeping dementia thereby contributing for poor nutritional intake.

The other answer choices describe less likely bone diagnoses in this patient.

Bone metastasis is less likely given the lack of known malignancy history and hypocalcemia on lab testing (vs. hypercalcemia more commonly associated with malignancy). Defective collagen synthesis describes the pathophysiology underlying osteogenesis imperfecta. which IS characterized by multiple fractures and most commonly presents early in life. Itis not associated with abnormalities of calcium and phosphorous metabolism. Paget disease usually characterized by multiple fractures an presents with near normal calcium and phosphate levels. Characteristic bone, features include mosaic architecture, long bone fractures, skull thickening, and increased risk of osteosarcoma Finally, parathyroid carcinoma would be expected to result hypercalcemia, rather than hypocalcemia seen in the patient.

5. **The answer is D.** A patient presents to autopsy with stiff musculature, consistent with rigor mortis. Rigor mortis occurs because the dead muscle cells are not regenerating their stores of ATP, which become depleted 3 to 4 hours after death. Without ATP being available to bind to myosin, actin cannot be released from myosin and the actomyosin complex is maintained, leading to rigidity of the muscles as they remain in a contracted state. By 72 hours after death, calcium-activated proteases and other enzymes are activated and begin hydrolysis of the muscle proteins, particularly the actomyosin complex, leading to flaccid condition of the muscle. Each of the other answer choices describes processes in muscle contraction, but these are not related to ATP-induced release of actin from myosin. Binding of actin to myosin, which is necessary for contraction, does not require ATP and would not explain the inability of the patient’s muscles to relax. Binding of troponin to tropomyosin is not correct, because troponin and tropomyosin are always bound to each other, and calcium rather than ATP affects the conformational changes of these associated proteins. The power stroke of the myosin is a downstream effect of ATP rather than a direct effect. The power stroke is mediated by release of inorganic phosphate (which result from hydrolysis of ATP), with the ADP then being displaced as ATP binds to the myosin head region . Finally, preventing uptake of calcium by the sarcoplasmic reticulum would increase the cytoplasmic concentration of calcium and increase muscle

contraction. Rigor mortis is not force production, but a stiffening of the muscle cells mediated by the absence of ATP rather than the presence of calcium, and its binding to troponin.

6. The answer is C. A sarcomere extends from one Z line to an adjacent Z line (see illustration below). A myofibril is made up of thin (actin-containing) and thick (myosin-containing) filaments. In some areas they overlap, and in other areas they do not. Thin filaments anchor on either side of the Z lines. The M line marks the center of a sarcomere and the thick filaments, and is located at the midpoint between Z lines. The I band contains only thin filaments, having no overlap with thick filaments, and each I band is centered on a Z line. The A band is centered on the M line and represents the full length of the thick filament, including both the H band and the region of overlap between actin and myosin. The H band is found in the central area of the A band, and contains only thick filaments, where they do not overlap with the thin filaments. The length of the A band never changes during contraction.The patient is experiencing a tonic-clonic seizure, which consists of a tonic phase (in which contraction is sustained) rhythmically). During muscle shortening, the power stroke of the myosin molecules in the thick filament results in thin filaments sliding on thick filaments (sliding filament mechanism) towards the center (M band) of the sarcomere, bringing Z lines closer together. The absolute length of the actin and myosin filaments in a myofibril does not change during shortening, but rather the overlap of the filaments increases. Thus, the A band does not change upon contraction. The H band and I band are the two areas where there is no overlap of myosin and actin, respectively; therefore, H and I bands will shorten when the overlap increases with contraction. Each of the alternative answer choices contains an incorrect pattern. As discussed, the A band spans the entire region containing thick filaments such that it is fixed and does not lengthen or shorten with the changing length of the muscle. During the power stroke, the actin fibers increase overlap and move closer to the M line. As a result, the H zone is shortened during contraction.

ANSWERS MCQs STEP 1

1. The correct answer is B. Normally, stretching of muscle results in a reflex contraction: the harder the stretch, the stronger the contraction. At a certain point, when the tension becomes too great, the contracting muscle suddenly relaxes. The reflex that underlies this sudden muscle relaxation is called the Golgi tendon organ (GTO) reflex, also known as the inverse stretch reflex or autogenic inhibition. The GTO is an extensive arborization of nerve endings (encapsulated by a connective tissue sheath and located near the muscle attachment) that is connected in series with the extrafusal skeletal muscle fibers. As a result, GTOs respond to muscle tension rather than muscle

length. Increased tension leads to stimulation of Ib afferents, which inhibit the homonymous muscle via spinal interneurons.

Free nerve endings (choice A) are unmyelinated, unencapsulated nerve endings that penetrate the epidermis. These types of receptors respond to pain and temperature.

Merkel disks (choice C) are composed of specialized tactile epidermal cells and their associated nerve endings. They are located in the basal layer of the epithelium and are slowly adapting receptors that respond to touch and pressure.

Muscle spindles (choice D) are spindle-shaped bundles of muscle fibers (intrafusal fibers) that are encapsulated by connective tissue. Muscle spindles are arranged in parallel with extrafusal skeletal muscle fibers, so they sense the length of the muscle. They are innervated by Group Ia and II sensory afferent neurons.

Pacinian corpuscles (choice E) are unmyelinated nerve endings surrounded by thin, concentric layers of epithelioid fibroblasts. In transverse section, this receptor resembles a sliced onion. They are found primarily in the deep layer of the dermis, loose connective tissue, male and female genitalia, mesentery, and visceral ligaments. They are rapidly adapting receptors that respond to touch and pressure.

2. **The correct answer is C.** This is a classic presentation of carpal tunnel syndrome, which typically affects women between the ages of 40 and 60 who chronically perform repetitive tasks that involve movement of the structures that pass through the carpal tunnel. One important structure that passes through the carpal tunnel is the median nerve. Patients often note tingling, loss of sensation, or diminished sensation in the digits. There is also often a loss of coordination and strength in the thumb, because the median nerve also sends fibers to the abductor pollicis brevis, flexor pollicis brevis, and the opponens pollicis. A final function of the median nerve distal to the carpal tunnel is control of the first and second lumbricals, which function to flex digits two and three at the metacarpophalangeal joints and extend interphalangeal joints of the same digits.

Abduction of the fifth digit (choice A) is a function controlled by the ulnar nerve, which does not pass through the carpal tunnel.

Adduction of the thumb (choice B) is a function of the adductor pollicis, which is the only short thumb muscle that is not innervated by the median nerve, but rather by the deep branch of the ulnar nerve. Sensation of the lateral half of the dorsum of the hand (choice D) is mediated by the radial nerve, which also does not pass through the carpal tunnel.

Sensation over the lateral aspect of the palm (choice E) is mediated by the median nerve; however, the branch innervating the palm (palmar cutaneous branch of the median nerve) passes superficially to the carpal tunnel.

Sensation over the medial aspect of the dorsum of the hand (choice F) is mediated by the ulnar nerve.

Sensation over the medial aspect of the palm (choice G) is mediated by the ulnar nerve.

3. The correct answer is B. During the contraction cycle, ATP binds to myosin cross-bridge heads, causing the dissociation of myosin from actin.

Actin (choice A) forms cross-bridges with myosin but does not bind to ATP.

The sarcoplasmic reticulum (choice C) is involved in storing and releasing Ca2+ for muscle contraction.

Tropomyosin (choice D) is a thin filament that runs alongside actin. In the absence of calcium, tropomyosin lies in the groove of the actin filament and blocks actin's myosin-binding sites.

Troponin C (choice E) is the calcium-binding subunit of the troponin complex. When troponin C binds calcium, a conformational change causes tropomyosin to shift, thereby exposing the myosin-binding sites on actin..

4. The answer is D. This disorder is usually associated with small cell carcinoma and results in muscle weakness. There is a reduction in size of the compound action potentials in affected muscles, but such effects can be partially reversed with exercise.

5. The answer is D. Titin is a large protein that connects the Z lines to the M lines, thereby providing a scaffold for the sarcomere. Titin contains two types of folded domains that provide muscle with its elasticity. The resistance to stretch increases throughout a contraction, which protects the structure of the sarcomere and prevents excess stretch.

6. The answer is B. Dystrophin is a large protein that forms a rod, which connects the thin filaments of actin to the transmembrane protein b-dystroglyan in the sarcolemma. b-Dystroglyan is connected to laminin in the extracellular matrix by a-dystroglyan. The dystroglycans are also associated with a complex of four transmembrane glycoproteins, called sarcoglycans. The dystrophin-glycoprotein complex adds strength to the muscle by providing a scaffolding for the fibrils and connecting them to the extracellular environment. Muscular dystrophy is the term used for some 50 diseases that cause progressive skeletal muscle weakness. Duchenne's and Becker's muscular dystrophy are two types resulting from mutations in the dystrophin gene.

7. The answer is D. Digoxin inhibits the sarcolemmal Na+, K+-ATPase ("sodium pump"). This reduces the active (ATP–dependent) extrusion of intracellular Na+. The relative excess of intracellular Na+competes with intracellular Ca2+for sites on a sarcolemmal 2Na–Ca exchange diffusion carrier, such that less Ca2+ is extruded from the cells. The net result is a rise of free [Ca2+] and greater actinmyosin interactions (i.e., a positive inotropic effect that increases cardiac output through an increase of stroke volume.

8. The answer is C. When there is danger of damage to the tendons or bones to which the muscles are attached, Golgi tendon organs are activated and elicit rapid responses through neural connections located within the spinal cord that result in muscle

relaxation. Golgi tendon organs are muscle proprioceptors that are found close to the junction between tendon and muscle fibers. They are in series with the muscle fibers and respond to the stretch of tendons which accompanies muscle tension. The threshold for activating them in this manner is high and it is therefore believed that they play an important role in the reflex response of a muscle after excessive force ("muscles give out"). In the spinal reflex pathways, the Ib afferent axons from the Golgi tendon organ synapse on inhibitory spinal cord interneurons, which then inhibit, not activate, alpha motor neuron activity serving the same muscles (choice A). Gamma motor neurons (choice B) innervate muscle spindles. These neurons control the sensitivity of the spindle by maintaining the proportions between spindle and muscle length and by dampening the function of the spindle, regardless of change in muscle length. This is important for normal movements. Muscle spindles (choice D) continuously signal information about the length of a muscle and the rate of change in length. They are important for conscious appreciation of the body's position, for planning and execution of controlled movements. Low oxygenation of the muscle or ischemia (choice E) is not the primary trigger for spinal reflexes, and will occur gradually, not suddenly as described in the question.

9. **The answer is D.** In smooth muscle, increased cytoplasmic [Ca2+] activates myosin light chain kinase, which acts to phosphorylate the light chain of the myosin molecule. Phosphorylation of the light chain activates myosin ATPase activity, initiating contraction. Troponin (choice E) is a calciumbinding protein that functions in both skeletal and cardiac muscles to regulate contractile activity. Troponin is not expressed in smooth muscle. Calcium (choice B) does regulate contractile activity. Increased intracellular [Ca2+] serves to activate contraction in both skeletal and smooth muscles. Myosin (choice C) and actin (choice A) are contractile proteins present in both skeletal and smooth muscles. Though essential to muscle contraction, these proteins function in contraction in both muscle types.

10. The answers is D. Elevated serum potassium levels cause membrane depolarization with a resulting Na-channel inactivation. Fibers are thus less able to fire action potentials, leading to impaired excitation contraction coupling, with muscle weakness (choice D is correct). Though hyperpolarization would also impede action potential generation, by moving the Na-channel away from its activation threshold, choices C and E are incorrect since high potassium causes membrane depolarization. Calcium required for skeletal muscle contraction is derived from internal stores (the sarcoplasmic reticulum) and is not dependent on calcium influx through surface membrane channels (choice B). There is no evidence that potassium interferes with the acetylcholine receptor (choice A). Hyperkalemia in this patient is probably due to multiple factors. Since insulin promotes potassium uptake into cells, too low an insulin dosage in the diabetic can lead to hyperkalemia. In addition, propranolol can cause a

shift of potassium from cell to blood. Finally, the elevated BUN indicates some renal failure, and failing kidneys cannot efficiently excrete potassium into the urine.

11. The answer is A. Tension generation depends on attachment of the myosin head group to actin, this is referred to as cross bridge formation. The amount of tension that can be generated in response to a stimulus depends, in part, on the number of cross bridge attachments that can be formed. Since myosin molecules form the thick filament and actin comprises the thin filament, as overlap between thick and thin filaments increases more myosin head groups can bind to actin and more cross bridges can form. Because of this, active tension generation depends on the extent of overlap of thick and thin filaments. Because skeletal muscle is quite compliant, very little passive tension is encountered until the muscle is stretched almost to its maximal length (choice C). During contraction neither the thick nor the thin filaments shortens (choice B). Contraction occurs as thick and thin filaments slide past each other. Velocity of shortening decreases with increasing load (choice E). In skeletal muscle, thin filaments attach to the Z line (choice D).

12. The answer is D. At the neuromuscular junction, an invading action potential opens voltage-gated calcium channels and Ca2+ enters the presynaptic terminal. Elevated cytoplasmic Ca2+ causes release of vesicles containing acetylcholine. Acetylcholine diffuses across the cleft and activates postsynaptic acetylcholine receptors with a resultant depolarization (the EPP). Lack of presynaptic calcium channels in LEMS means that less Ca2+ enters the terminal of the presynaptic membrane—therefore less transmitter is released and the size of the EPP is decreased. Postsynaptic properties, neither action potential threshold nor size are altered due to the deficit of presynaptic calcium channels in LEMS (choices Aand B). The MEPPis due to spontaneous transmitter release. The amplitude depends on the amount of transmitter in each vesicle. Lack of presynaptic calcium channels will not affect the size of the MEPP, since each vesicle still has the same amount of transmitter (choice C). Quantal content is the amount of transmitter per vesicle which, as described above, will not be altered in LEMS (choice E).

13. The answer is B. Cardioactive steroids inhibit the Na, KATPase present in the plasma membrane of the cardiac muscle cell. At the therapeutic dosages that are employed, there will be partial ATPase inhibition with decreased active sodium efflux from the myoplasm and a resultant increase in myoplasmic sodium ion concentration. Due to increased intracellular sodium concentration the Na:Ca exchange protein (NCX) can extrude less calcium from the cell and the intracellular concentration of calcium will increase. This increases force, since contractile force depends on calcium. Though calcium influx through Ntype calcium channels is also an important source of calcium to regulate contraction, calcium channel activity is not regulated by the cardioactive steroids (choice A). Similarly, neither potassium (choice D) nor sodium

(choice E) channels are immediately involved in the mechanism of action of digoxin. PMCA (choice C) acts in cardiac muscle to pump calcium out of the cell, thereby helping to maintain a low myoplasmic [Ca2+]. However, PMCAactivity is not directly involved in the mechanism of action of digoxin.

14. The answer is D. Malignant hyperthermia is caused by a mutation to the calcium release channel of the skeletal muscle sarcoplasmic reticulum (the socalled ryanodine receptor). Increased calcium release into the myoplasm causes strong, sustained skeletal muscle contraction. This causes excessive ATPhydrolysis, increased metabolic activity to replenish ATP levels, heat generation, and carbon dioxide production. Decreased acetylcholine release would decrease muscle contraction (choice A). Myosin light chain kinase is involved in contractile activation in smooth muscle (choice B). Activation of K channels would hyperpolarize muscle fibers and tend to decrease susceptibility to contractile activation (choice C). Inhibition of sodium channels would diminish the ability of skeletal muscle to generate action potentials and thus decrease excitability (choice E).

CLINICAL CASES

1. A 3-year-old boy is brought to the pediatrician by his parents because he has been falling frequently and struggling to get up from a sitting or lying position, whereas he had previously done so with ease. His developmental history is notable for delayed motor skills; he began to walk at 18 months. The boy has a waddling gait and when sitting uses his arms to push himself into the upright position (Figure 9-7). Physical examination shows marked muscle weakness of the extremities, particularly of the proximal muscle groups, and hypertrophy of his calf muscles. The patient's maternal uncle, who died at 16 years of age, suffered from similar symptoms when he was younger.

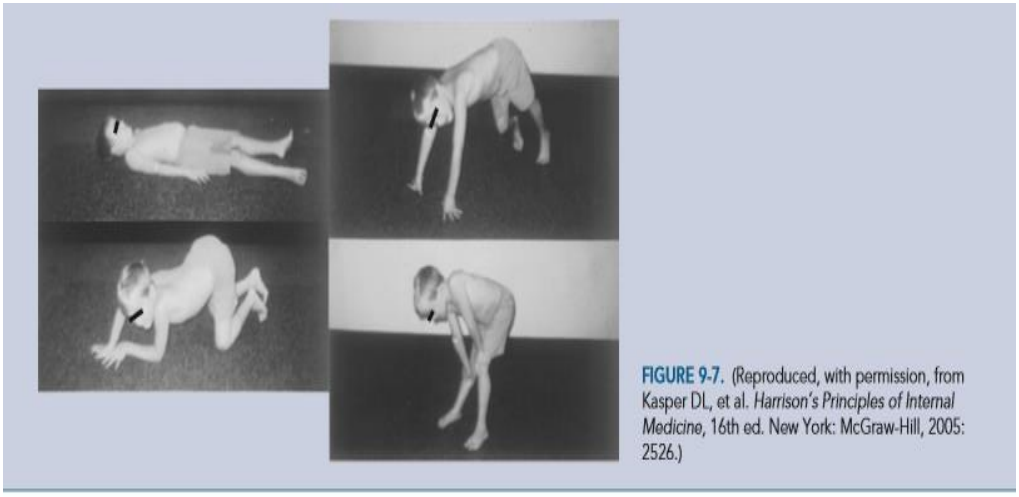


FIGURE 9-7. (Reproduced, with permission, from Kasper DL, et al. *Harrison's Principles of Internal Medicine*, 16th ed. New York: McGraw-Hill, 2005: 2526.)

Reproduced from First Aid cases for USMLE STEP 1

1.1 What is the likely diagnosis and what is the pathogenesis of the disorder?

Duchenne muscular dystrophy (DMD) is an X-linked recessive (Xp21) disorder marked by a deficiency of functional dystrophin, a 23,000-kB protein that helps stabilize muscle fibers. approximately one-third of cases are sporadic and due to spontaneous mutations (noninherited) that arise from a misalignment of chromosomes for USMLE a recombination event.

1.2 What is the prognosis for patients with this condition?

Patients with DMD are usually unable to walk by the end of the first decade and are confined to a wheelchair by 12 years of age. Most patients die by the end of the second decade; respiratory failure is the leading cause of death. Dilated cardiomyopathy and/or conduction abnormalities are common and can be fatal.

1.3 What tests are used to diagnose this condition?

If DMD is clinically suspected, serum creatine kinase levels are markedly elevated, and electromyography shows myopathic changes, genetic testing or a muscle biopsy can confirm the diagnosis. Muscle biopsy shows atrophic muscle fibers of various sizes in disarray, degeneration, and necrosis of individual muscle fibers with fibrous replacement.

1.4 Which band in a sarcomere stays constant in length during muscle contraction?

The A band, which corresponds to the length of the thick myosin filaments.

2. A 62-year-old woman presents to her clinician with joint pain and morning stiffness for the past few years. The joint pain is present in both hands and feet bilaterally and has caused significant deformity and weakness. On physical examination, these joints are tender to palpation, warm, and swollen with no erythema. Her metacarpal joints display ulnar deviation bilaterally and subcutaneous nodules can be palpated at the elbow.

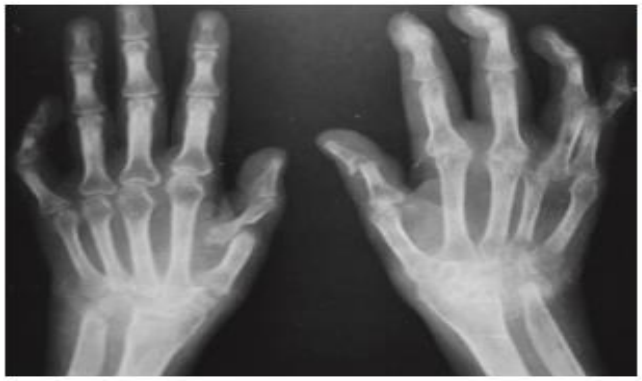


FIGURE 9-9. Radiographic changes in rheumatoid arthritis. Severe destruction of radiocarpal articulation with subluxation and ulnar deviation at the wrist; loss of ulnar styloid bilaterally; dislocation of the proximal interphalangeal joint of the left thumb and dislocation of the right fourth and fifth finger metacarpophalangeal joints and left metacarpophalangeal joint; diffuse joint space narrowing of many interphalangeal joints. (Reproduced, with permission, from Brunicardi FC, et al. *Schwartz's Principles of Surgery*, 8th ed. New York: McGraw-Hill, 2005: 1679.)

Reproduced from First Aid cases for USMLE STEP 1

2.1 What is the pathophysiology of this condition?

RA is a chronic systemic autoimmune inflammatory disorder that destroys articular cartilage. While the etiology is unclear, the autoimmune reaction is mediated by CD4+ t cells, macrophages, and cytokines (tumor necrosis factor and interleukin-1), which promote the inflammatory response. together these elements form a pannus that gradually erodes and disfigures joints.

2.2 What joints are typically affected in this condition?

Symptoms usually develop symmetrically in the small joints of the hands and feet (metacarpophalangeal, proximal interphalangeal, metatarsophalangeal joints), as well as wrist, elbows, knees, and ankles. the cervical spine may also be involved.

2.3 What are the characteristic joint deformities in this condition?

Ulnar deviation/drift, swan-neck, and Boutonniere deformities of the fingers and the "bow-string" sign (prominence of the tendons in the extensor compartment of the hand) are all characteristic of ra. Occasionally patients present with synovial cysts from increased intra-articular pressure and eventual tendon rupture.

2.4 What are the primary pharmacologic therapies for this condition?

Analgesics including acetaminophen. Nonsteroidal anti-inflammatory drugs. Glucocorticoids. Disease-modifying antirheumatic drugs such as methotrexate, hydroxychloroquine, or sulfasalazine. Anti-cytokine therapies such as etanercept, infliximab, and adalimumab. Other biologic agents such as abatacept and rituximab.

3. A 65-year-old woman presents to the emergency department with sharp pain in her lower back after lifting some heavy objects while moving into a new home. The pain

radiates to the anterior abdomen and is exacerbated by sitting and moving. On physical examination, she appears kyphotic with a “dowager hump.” A plain film radiograph reveals multiple vertebral compression fractures.

3.1 What underlying condition contributed to these fractures?

Osteoporosis. this disease is characterized by reduced bone mass with microarchitectural disruption, porosity, and skeletal fragility. Osteoporosis is difficult to diagnose, as a fracture is often the first clinical manifestation.

3.2 What two factors contribute most to this condition?

The majority of postmenopausal women with osteoporosis have bone loss related to age and/or estrogen deficiency. estrogen naturally suppresses cytokines (such as interleukin-1 and -6) and receptor activator of nuclear k-B ligand (raNKL,) which both increase osteoclast activity. raNKL interacts with raNK to promote development and function of osteoclasts. Denosumab is the first osteoporosis treatment that acts by blocking raNK-raNKL binding.

3.3 What secondary factors increase the risk of this condition?

Physical inactivity. Calcium and vitamin D deficiency. Prolonged glucocorticoid therapy. Hyperparathyroidism. Hyperthyroidism.

3.4 What tests and/or imaging tools can be used to test bone density?

Dual-energy x-ray absorptiometry (DEXA) scans are used to compare bone density to an age-matched reference population. Density more than two standard deviations below the expected range confirms the diagnosis.

3.5 What are the appropriate treatments for this condition?

The mainstay of treatment and prevention of osteoporosis is bisphosphonates such as alendronate and risedronate. this is in addition to continuation of both calcium and vitamin D supplementation. these agents act by decreasing osteoclastic bone resorption. One of the side effects of bisphosphonates is esophagitis; thus, patients are instructed to take it with water and while standing or sitting upright (and remain so for at least 30 minutes). Raloxifene, a selective estrogen receptor modulator is also used in refractory cases. Intermittent administration of recombinant parathyroid hormone has also shown to be effective.

4. A 16-year-old boy is brought to the emergency department via ambulance after a motor vehicle accident. Physical examination reveals obvious trauma to the chest, and the patient is tachypneic and hypotensive. X-ray of the chest shows a hemothorax, and a chest tube is placed on the right.

4.1 What conditions should be considered in a patient with trauma to the chest

Direct injury can cause pulmonary or myocardial contusion, rib or sternal fractures, diaphragmatic injury, vessel laceration, and aortic damage, which is often fatal. Conditions associated with chest trauma include pneumothorax, flail chest, hemothorax, and cardiac tamponade.

4.2 What important nerves are at risk in stab wounds to the thorax?

Cardiac plexus. Recurrent laryngeal nerve. phrenic nerve. Pulmonary plexus (contiguous with the cardiac plexus). Vagus nerve.

4.3 What are the major arteries and veins of the thorax?

Arterial Supply aortic arch Brachiocephalic trunk Common carotid Internal thoracic Internal thoracic Left bronchial Subclavian Venous Supply azygos Brachiocephalic Internal thoracic Jugular.

4.4 What is the difference between the left and right mainstem bronchi?

the mainstem bronchus passes inferolaterally from the bifurcation of the trachea at the sternal angle to the hilum. the right main bronchus is shorter and wider and runs more vertically, allowing for passage of aspirates more easily than the left bronchus. the left main bronchus is longer and travels anterior to the esophagus between the thoracic aorta and the left pulmonary artery.

4.5 What are the clinical features in a patient with pneumothorax post trauma?

Fractured ribs from trauma or trauma itself can lead to a pneumothorax. patients will often be tachypneic, hypoxic, and/or have decreased/absent breath sounds on the side of the pneumothorax. Imaging can confirm a pneumothorax. a chest tube is usually used to manage a pneumothorax from trauma. If there is a pneumohemothorax, separate chest tubes should be used to remove the blood and the air.

5. A 24-year-old woman presents to the clinic complaining of fatigue, muscle and joint aches, and intermittent fevers of over 2 months' duration. On physical examination, she displays a rash over her cheeks and nose as well as a friction rub on cardiac auscultation. Laboratory tests show the following: Hemoglobin: 10.8 g/dL Hematocrit: 32.8% Platelet count: 145,000/mm3 WBC count: 4350/mm3 Urinalysis: 3+ proteinuria

5.1 What is the most likely diagnosis?

Systemic lupus erythematosus (SLE). SLe is a multisystem autoimmune connective tissue disease with a variable clinical presentation that most commonly affects young women in their 20s and 30s. Most manifestations of SLE are secondary to immune complex deposition.

5.2 What explains the friction rub on auscultation?

SLe patients can develop pericarditis leading to friction rub.

5.3 What laboratory tests can be used to confirm the diagnosis?

Antibody testing including antinuclear antibodies (aNa), antiphospholipid antibodies, antibodies to double-stranded DNa (dsDNa), and anti-Smith (Sm) antibodies are used to diagnose SLE. positive antidsDNa and anti-Sm test results are the most specific for SLE. a positive aNa test is sensitive but not specific. high-yield fact: antiphospholipid antibodies also bind the cardiolipin antigen used in syphilis testing; therefore, lupus patients have a false-positive syphilis test.

5.4 What would a positive antihistone antibody suggest?

It would suggest drug-induced lupus, but the reason for this correlation is unknown. Common medications that can cause drug-induced lupus include hydralazine, procainamide, minocycline, penicillamine, and isoniazid.

5.5 What are the typical renal findings in this condition?

Most SLe patients have an abnormal urinalysis. there are six classes of renal disease in SLE, which are usually differentiated with a renal biopsy. Immune complex (anti-DNa-DNa)–mediated glomerular diseases are most common. SLE nephropathy most commonly displays a nephrotic syndrome pattern with a histologic subtype of diffuse lupus nephritis (class IV). the pathologic finding on histology that is almost pathognomonic for SLE is “wire loop” lesions (tubuloreticular structures in the glomerular endothelial cells, which may also be seen in hIV nephropathy). Other findings include subepithelial or subendothelial deposits with inflammation.

6. A 54-year-old woman presents to the clinic with fatigue, difficulty swallowing, a nonproductive cough, stiffness in the joints of her hands, and tightness in her fingers. Additionally, she explains that her fingers occasionally become pale and painful when she forgets to wear gloves on cold days. On physical examination, her skin is taut and thickened over her hands and face. Her hands appear clawlike and have decreased motion at all of the small joints symmetrically.

6.1 What is the most likely diagnosis and what are the two forms of this condition?

Systemic sclerosis (scleroderma), an autoimmune connective tissue disorder. Scleroderma exists in two forms, limited and diffuse, both of which occur in the setting of raynaud phenomenon (exaggerated vasoconstriction in response to cold or stress leading to sharply demarcated color changes of the fingertips). this patient displays the limited form in which the skin of the fingers, forearms, and face are often affected with distinctive thickening. Diffuse systemic sclerosis eventually involves visceral organs as well as the gastrointestinal tract (particularly the esophagus), heart (myocardial fibrosis), muscles, lungs (interstitial lung disease is seen in the majority of patients, causing dyspnea on exertion and cough), and kidneys. this results in dysphagia, respiratory difficulty, arrhythmias, and mild proteinuria. the most concerning manifestation of this disease is malignant hypertension leading to renal failure.

6.2 What serologic marker is used to test for this condition?

anti-DNa topoisomerase I (Anti-Scl-70) antibody is highly specific for systemic sclerosis. anticentromere antibodies are more characteristic of limited scleroderma (CreSt syndrome).

6.3 What is the pathogenesis of this condition?

the etiology of this condition is unknown; however, symptoms begin with vascular damage and are due to excessive synthesis of extracellular matrix, increased deposition of collagen in normal tissue, fibrosis, immune activation, and vascular damage.

6.4 What is CREST syndrome?

CREST is an acronym for the five findings in individuals with limited systemic sclerosis: Calcinosis, Raynaud phenomenon, Esophageal dysmotility, Sclerodactyly, and Telangiectasia.

6.5 What is the appropriate treatment for this condition?

Most therapies are supportive; skin-softening agents and gloves are used to help skin sclerosis and raynaud phenomenon. Bosentan and prostacyclin analogs might also be useful in pulmonary hypertension. Cytotoxics have a role in treating inflammatory lung disease.

SECTION NERVOUS SYSTEM
Physiology of nerves and synapses
MCQs STEP 1

1. A neurophysiologist is studying the functional properties of various receptor subtypes, using whole-cell voltage clamp recordings made from coronal brain slices. At a holding potential of −70 mV, bath application of receptor agonists for four different receptor types consistently elicited either excitatory postsynaptic currents or inhibitory postsynaptic currents. During the study of one receptor, however, agonist application failed to elicit a postsynaptic response at −70 mV but did elicit a reliable response at a holding potential of 0 mV. This receptor is most likely which of the following?

A. Gamma-amino-butyric acid (GABA)A
B. Kainate
C. Nicotinic acetylcholine
D. N-methyl-D-aspartate (NMDA)
E. Serotonin 3 (5-HT3)

2. A woodworker operating a band saw accidently injures his wrist, severing his radial artery and producing severe hemorrhage. As he loses blood, his body tries to compensate for the developing hypotension by increasing sympathetic outflow. The postganglionic signals carrying the impulses to constrict his arterioles are transmitted along which of the following fiber types?

A. A-δ fibers
B. B fibers
C. C fibers
D. Ia fibers
E. Ib fibers

3. A patient with a family history of peripheral neuropathy is found to have a decrease in nerve conduction velocity and an X-linked mutation of connexin 32, consistent with Charcot-Marie-Tooth Disease. Connexin is an important component of which of the following?

A. Gap junction
B. Sarcoplasmic reticulum
C. Microtubule
D. Synaptic vesicle
E. Sodium channel

4. A 30-year-old woman with partial seizures is treated with vigabatrin. Which of the following is the principal mechanism of action of vigabatrin?

A. Sodium channel blockade

B. Increase in frequency of chloride channel opening
C. Increase in GABA
D. Calcium channel blockade
E. Increased potassium channel permeability
F. NMDA receptor blockade
5. A patient with temporal lobe epilepsy is treated with a drug designed to inhibit the principal cell type responsible for the seizures. Which of the following cell types is targeted by this drug?
A. Basket cell
B. Purkinje cell
C. Stellate cell d
D. Schwann cell
E. Pyramidal cell
6. A patient receives a single injection of succinylcholine to facilitate preoperative intubation. The dose is correct for the vast majority of patients, and normally effects of this drug abate spontaneously over a couple of minutes. This gentleman remains apneic for an extraordinarily long time. A genetically based aberrant cholinesterase is eventually determined to be the cause. Which of the following would we administer if we were concerned about this unusually lengthy drug response?
A. Atropine
B. Bethanechol
C. Neostigmine
D. Nothing
E. Physostigmine
F. Tubocurarine
7. A 42-year-old woman consults a dermatologist to evaluate and treat her glabellar lines (frown lines on the forehead just above the nose). After her treatment options are explained, the patient asks the dermatologist to administer Botox (botulinum type A). Botox injections smooth out glabellar lines by which of the following methods?
A. Blocking the release of synaptic transmitter from a-motoneurons
B. Preventing the opening of sodium channels on muscle membranes
C. Decreasing the amount of calcium released from the sarcoplasmic reticulum
D. Increasing the flow of blood into the facial muscle
E. Enhancing the enzymatic hydrolysis of acetylcholine at the neuromuscular junction
8. A patient who has been treated for Parkinson’s disease for about a year presents with purplish, mottled changes to her skin. Which of the following drugs is the most likely cause?
A. Amantadine
B. Bromocriptine

C. Levodopa (alone)
D. Levodopa combined with carbidopa
E. Pramipexole
9. A newborn male is evaluated because of inability to breast feed and found to have severe hypotonia (low muscle tone). The child lays in a frog leg posture with minimal spontaneous movements, and the head and legs dangle to the bed when suspended by his stomach. A large anterior fontanel is noted, and initial laboratory tests indicate elevated liver enzymes. The physician suspects Zellweger syndrome (214100), an end phenotype reflecting peroxisome dysfunction that may be caused by mutations in several different peroxisomal membrane protein genes. The diagnosis is confirmed by demonstrating elevated plasma levels of very long chain fatty acids and of erythrocyte plasmalogens. Which of the following compounds is the starting point of ether lipid and plasmalogen synthesis?
A. Acetyl CoA
B. Pyruvate
C. Dihydroxyacetone phosphate
D. Malonyl CoA
E. Palmitoyl CoA
10. A child is suffering from a developmental abnormality that affects the primary transmitter released from terminals of both neostriatal and paleostriatal neurons. Which neurotransmitter is most likely affected by this abnormality?
A. Glycine
B. Enkephalin
C. Dopamine
D. GABA
E. Glutamate
11. We have a 48-year-old female patient with a history of myasthenia gravis. She has been treated with an oral acetylcholinesterase inhibitor for several years, and has done well till now. She presents with muscle weakness and other signs and symptoms that could reflect either a cholinergic crisis (excess dosages of her maintenance drug) or a myasthenic crisis (insufficient treatment). We will use a rapidly acting parenteral acetylcholinesterase inhibitor (AChE) to help make the differential diagnosis. Which of the following drugs would be most appropriate for this use?
A. Edrophonium
B. Malathion
C. Physostigmine
D. Pralidoxime
E. Pyridostigmine

12. A young woman in her early twenties experiences loss of sensation in her legs and weakness in her limbs. A neurological examination further indicated some spasticity of the limbs as well. The neurologist provided a preliminary diagnosis of onset of multiple sclerosis (MS). Assuming that this diagnosis is correct, which of the following best accounts for the diminution of sensory and motor functions?

A. Loss of Schwann cells in peripheral neurons

B. An overall loss of dopaminergic release throughout the brain and spinal cord

C. Loss of peripheral cholinergic neurons

D. Demyelination of CNS neurons

E. Proliferation of oligodendrocytes

13. Multiple sclerosis is a relatively common nervous system demyelinating disease. It is autoimmune and restricted to the central nervous system. Nerve conduction velocity is depressed in almost all affected individuals. Manipulations which prolong action potential duration seem to mitigate symptoms, possibly by facilitating conduction through sections of membrane which are no longer myelinated. Application of which type of drug might be expected to prolong action potential duration and thus be a potential therapeutic tool?

A. Activates potassium channels

B. Blocks l-type calcium channels

C. Blocks potassium channels

D. Blocks sodium channels

E. Increases sodium channel inactivation

14. Gamma-aminobutyric acid (GABA) is an amino acid that functions as a neurotransmitter in the central nervous system. GABA typically causes increased chloride conductance and functions as an inhibitory transmitter. Assume that the equilibrium potential for chloride (ECl^-) in a particular cell is −80 mV and that application of GABA inhibits the cell without any change in resting membrane potential. What is the resting membrane potential of the cell?

A. +80 mV

B. 0 mV

C. −70 mV

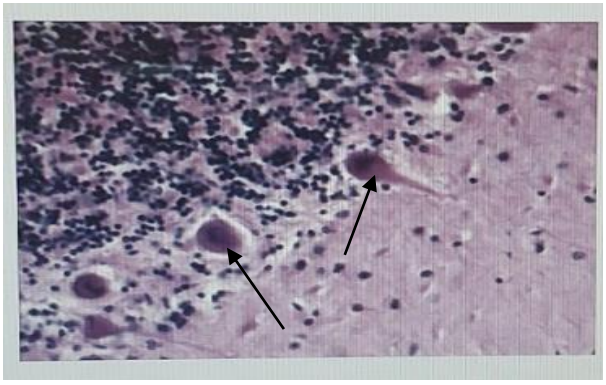
D. −80 mV

E. −90 mV

MCQs IFOM

1. The image shown is a photomicrograph depicting normal cerebellar architecture. The large cells in the image integrate the cerebellar cortical activity and transmit that information to the deep cerebellar nuclei. Which of the following neurotransmitters is used by the large integrating neurons?

Which of the following neurotransmitters is used by the large integrating neurons?



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A. y-Aminobutyric acid
B. Acetylcholine
C. Dopamine
D. Glutamate
E. Glycine

ANSWERS MCQs STEP 1

1. **The correct answer is D.** The NMDA receptor, a type of glutamate receptor, is unique in that it is both voltage- and ligand-gated. In other words, it requires both an agonist and neuronal depolarization to be activated. The NMDA receptor is an ion channel that allows the passage of Na+ and Ca2+ when open. At resting membrane potential, the channel is plugged by a Mg2+ ion. Depolarization (and agonist activation) causes the Mg2+ ion to dislodge, allowing the receptor to be functional. The GABAA receptor (choice A) is a ligand-gated chloride channel. The kainate receptor (choice B), a type of glutamate receptor, the nicotinic acetylcholine receptor (choice C), and the 5-HT3 receptor (choice E) are ligand-gated Na+ channels.

2. The correct answer is C. There are two systems currently used for classifying nerve fibers. The first system groups both sensory and motor fibers together, describing A-α, A-β, A-γ, A-δ, B, and C fibers. Another system relates only to sensory fibers, describing Ia, Ib, II, III, IV categories. Both classification schemes begin with large, myelinated fibers, progressing to finer, unmyelinated fibers. The C fiber (or IV fibers) is the only type of fiber that is unmyelinated. Remember that preganglionic neurons are myelinated, but postganglionic neurons are unmyelinated. Neurons that carry slow pain and temperature information are also classified as C fibers. See the table below for more information.

Sensory and motor fibers	Sensory fibers	Function
A-α	Ia (choice D)	Alpha motor neurons, primary afferents of muscule spindles
A-α	Ib (choice E)	Golgi tendon organ afferents, touch and pressure
A-β	II	Secondary afferents of muscle spindles, touch and pressure
A-γ		Gamma motor neurons
A-δ	III (choice A)	Touch, pressure, pain and temperature (fast)
B	(choice B)	Preganglionic autonomic, visceral afferents
C	IV (choice C)	Postganglionic autonomic

3. The answer is A. Connexin is a membrane-spanning protein that is used to create gap junction channels. The gap junction channel creates a cytoplasmic passage between two cells. Each cell membrane contains half of the channel. The channel, called a connexon, is constructed from six connexin molecules that form a cylinder with a pore at its center. Charcot-Marie-Tooth (CMT) disease comprises a heterogeneous group of inherited peripheral neuropathies. Approximately 1 in 2500 persons has some form of CMT, making it one of the most frequently occurring inherited neurological

syndromes. Transmission is most frequently autosomal dominant but it may also be autosomal recessive or X-linked, like the mutation affecting the connexin 32 (Cx32), located in the folds of the Schwann cell cytoplasm around the nodes of Ranvier. This localization suggests a role for gap junctions composed of Cx32 in ion and nutrient transfer around and across the myelin sheath of peripheral nerves.

4. The answer is C. Vigabatrin (γ-vinyl GABA) is useful in partial seizures. It is an irreversible inhibitor of GABA aminotransferase, an enzyme responsible for the termination of GABA action. This results in accumulation of GABA at synaptic sites, thereby enhancing its effect.

5. The answer is E. The pyramidal cell is a cell in the cortex that uses glutamate, an excitatory neurotransmitter, whereas most other types of cortical neurons use GABA, an inhibitory neurotransmitter. The spike, one identifying feature of an epileptic seizure seen on an EEG recorded on the scalp, is initiated by a depolarization shift, which is thought to be generated by EPSPs.

6. The answer is D. While this may seem like a trick question, the point is that even with markedly deficient cholinesterase activity, the succinylcholine eventually will be metabolized and its effects will disappear. All that needs to be done is to maintain adequate mechanical ventilatory support. Succinylcholine exerts its effects by activating nicotinic receptors on skeletal muscle (powerfully but normally briefly, owing to prompt metabolism) and depolarizing the myocytes. Atropine will not work. It blocks only muscarinic receptors. Bethanechol is a muscarinic agonist. Although it may have some nicotinic activating actions at extraordinarily high doses, that effect would add to, not resolve, the effects of the succinylcholine. Some texts note that under some conditions succinylcholine can cause what is termed Phase II block: a type of neuromuscular blockade that is curare-like (i.e., nondepolarizing). Because nondepolarizing blockade can be (and is, clinically) reversed with acetylcholinesterase inhibitors (mainly neostigmine; physostigmine would work but is not used because of its CNS effects), the implication is that we could administer a cholinesterase inhibitor here and reverse the paralysis. However, this so-called Phase II block is a manifestation of excessive (toxic) doses of succinylcholine and is not likely to apply here. Regardless, the approach is to give nothing and to ventilate the patient as long as needed, as noted.

7. The answer is A. Botulinum toxin inhibits the release of acetylcholine from a-motoneurons by blocking one of the proteins responsible for the fusion of the synaptic channel with the presynaptic membrane. Botulinum toxin also inhibits the release of acetylcholine from the neurons of the autonomic nervous system. Botulinum and tetanus toxin are released from the same class of bacteria (Clostridium). Tetanus toxin produces an increase in skeletal muscle contraction by blocking the release of inhibitory neurotransmitter from spinal interneurons.

8. The answer is A. This cutaneous response, called livedo reticularis, is characteristically associated with amantadine. Recall that this seldom-used antiparkinson drug probably works by releasing endogenous dopamine and blocking its neuronal reuptake. Livedo reticularis is not associated with levodopa (used alone or with carbidopa; c or d), nor with the dopamine agonists bromocriptine (d) or pramipexole (e; a newer and generally preferred drug for starting treatment of mild parkinsonian signs and symptoms). (You might also recall that amantadine is also used for prophylaxis of some strains of influenza virus infections.)

9. The answer is C. Triacylglycerols are assembled from glycerol and saturated fatty acids that are synthesized from condensation of malonyl and acetyl CoA through the fatty acyl synthase complex. Plasmalogens and certain signaling agents like platelet activating factor are ether lipids, distinguished by an ether (C-O-C) bond at carbon 1 of glycerol. Ether lipid synthesis is initiated by placing an acyl group on carbon 1 of dihydroxyacetone phosphate (DHAP) using DHAP acyltransferase. The acyl side chain is then exchanged with an alcohol to form an ether linkage by an acylDHAP synthase—the acyltransferase and synthase plus other enzymes of ether lipid synthesis are localized in peroxisomes. Subsequent additions of phosphocholine yield ether/acyl glycerols analogous to lecithins (including platelet activating factor), and addition of a phosphoethanolamine to carbon 3 of ether (alkyl) glycerols forms plasmalogens. Acetyl and palmitoyl CoA can contribute to these ether lipid modifications after the core carbon 1 ether linkage has produced an alkylglycerol. Disruption of peroxisome structure by mutations in various peroxisomal membrane proteins ablates DHAP acyltransferase and other enzymes for ether lipid/plasmalogen synthesis, causing deficienty of brain lipids, severe neurologic disease, hypotonia, and liver failure—the most severe phenotype of which is Zellweger syndrome (214100).

10. The answer is D. The major transmitter released at terminals of neostriatal and paleostriatal fibers is GABA. Thus, the output of the basal ganglia is mainly inhibitory. This suggests that thalamic influences upon the cortex are generated through the process of disinhibition, whereby neurons of the basal ganglia are inhibited. The presence of glycine in striatal neurons has yet to be demonstrated. Enkephalins are released from terminals of neostriatal-pallidal fibers but not from other efferent neurons of the striatum. Dopamine is released from the brainstem and some adjoining hypothalamic neurons but certainly not from striatal neurons. The neostriatum receives cortical inputs that utilize glutamate, but the release of GABA from terminals of neostriatal efferent fibers has not been demonstrated.

11. The answer is A. Although several of the listed drugs inhibit the activity of AChE, only edrophonium is used in the diagnosis of myasthenia gravis. The drug has a more rapid onset of action (1 to 3 min following intravenous administration) and a shorter duration of action (approximately 5 to 10 min) than pyridostigmine. This fast

acting/short duration profile is precisely what we want in this situation. We can quickly get our diagnostic answer, yet not have to deal too long with adverse responses (such as ventilatory paralysis) if the patient was experiencing a cholinergic crisis (excessive doses of their oral cholinesterase inhibitor); and we've now worsened the situation by inhibiting the metabolic inactivation of ACh even more with our diagnostic medication. (The short duration and the need for parenteral administration preclude use of edrophonium as a practical drug for long-term treatment of myasthenia gravis.) Malathion (b) is used topically to treat head lice and is never used internally (intentionally). Pyridostigmine (e) is used orally for maintenance therapy of myasthenia gravis. Physostigmine (c) is indicated for treatment of glaucoma (given topically), and is also a valuable parenteral drug for treating toxicity of anticholinergic drugs such as atropine. They are all cholinesterase inhibitors. Pralidoxime (d) is a "cholinesterase reactivator" and is used adjunctively (with atropine) in the treatment of poisonings caused by "irreversible" cholinesterase inhibitors, such as the "nerve gases" used as bioweapons and some commercial insecticides.

12. The answer is D. Multiple sclerosis is a demyelinating disease. The lesions may also involve some reactive gliosis and axonal degeneration as well. It occurs mainly in the white matter of the spinal cord and brain as well as in the optic nerve.

13. The answer is C. In clinical trials, a class of drugs, the aminopyridines, that blocks certain potassium channels has shown some promise for symptomatic relief of the symptoms of multiple sclerosis. The neuronal action potential is terminated by sodium channel inactivation and potassium channel activation. A drug that blocks potassium channels would thus prolong the action potential. Activating potassium channels (choice A) or increasing sodium channel inactivation (choice E) would shorten the action potential. Blocking sodium channels (choice D) would either shorten the action potential or block it altogether. Since calcium channels are not involved in the neuronal action potential, calcium channel blockade would not be expected to have much effect (choice B).

14. The answer is D. This problem addresses two issues: (1) the mechanism of action of inhibitory neurotransmitters and (2) the relationship of equilibrium potential and membrane potential. First, an inhibitory neurotransmitter acts by increasing conductance of an ion the equilibrium potential of which is either equal to or more negative than the cell resting membrane potential. If the equilibrium potential of the ion is more negative than the resting membrane potential, increasing the conductance of that ion will hyperpolarize the membrane—will generate an inhibitory postsynaptic potential (IPSP). Second, if the equilibrium potential of the ion is equal to resting membrane potential, increasing the conductance of that ion will "clamp" the membrane potential more tightly at its resting level—this will make the cell less excitable. In this problem, the membrane potential must equal −80 mV (D). If, and only if, the resting

membrane potential equals the equilibrium potential for an ion, will an increase in the conductance to that ion not cause a change in membrane potential.

ANSWERS MCQs IFOM

1. The correct answer is A. The question shows an image of a normal cerebellum and is asking about the large cells transmitting cerebellar cortical activity to deep cerebellar nuclei. The cells in question (circled) are Purkinje cells. Since Purkinje cells are inhibitory cells in the cerebellum, they primarily release GABA or y-Aminobutyric acid (an inhibitory neurotransmitter) onto the neurons of the deep cerebellar nuclei. Acetylcholine and glutamate are excitatory neurotransmitters, which would not be used by the inhibitory Purkinje cells. Dopamine can be either excitatory or inhibitory depending on the receptor subtype but it is not used by Purkinje cells. Glycine is an inhibitory neurotransmitter but it is primarily inhibiting neurons in the spinal cord and is not used by Purkinje cells in the deep cerebellar nuclei.

CLINICAL CASES

1. 73-year-old well-educated woman is brought to the physician by her daughter, who has become concerned about her mother's behavior. The mother volunteers at the local library shelving books, but for the past few months she has had trouble remembering where the books go. In addition, she often forgets to turn the stove off after cooking her family's long-time favorite dishes.

1.1 What is the most likely diagnosis?

This history is consistent with alzheimer disease, which is characterized by loss of short-term memory and general preservation of long-term memory.

1.2 How are the causes of dementia classified?

Dementia is classified into reversible and irreversible causes. reversible causes include major depression, hypothyroidism, and chronic subdural hematoma. Other irreversible causes are vascular dementia, normal pressure hydrocephalus, and dementia with Lewy bodies.

1.3 What risk factors are associated with this condition?

Advancing age and a family history of alzheimer disease are two well-known risk factors. additionally, because the amyloid precursor protein (app) is located on chromosome 21, patients with Down syndrome (trisomy 21) have increased app levels; these patients often develop alzheimer disease at 30–40 years of age. presenilin 1 is located on chromosome 14 and is noteworthy for its association with early-onset alzheimer disease. abnormalities in this gene result in increased β-amyloid accumulation.

1.4 What are the likely gross pathology findings in this condition?

Neurofibrillary tangles and amyloid plaques are commonly seen on autopsy. A high degree of cerebral atrophy in the frontal, temporal, and parietal regions is also present.

1.5 What biochemical mechanism is likely involved in the pathogenesis of this condition?

A preferential loss of acetylcholine and choline acetyltransferase in the cerebral cortex may play a role in the development of clinical disease.

1.6 What is the most appropriate treatment for this condition?

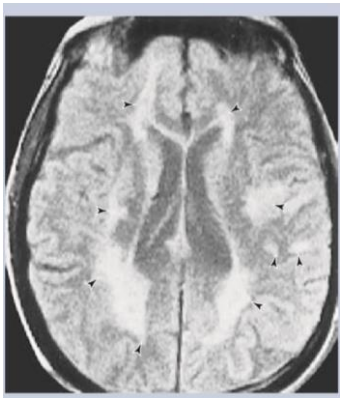
The acetylcholinesterase inhibitor class of medications, including tacrine, donepezil, rivastigmine, and galantamine, have been shown to slow the progress of memory loss. Memantine, an N-methyl-d-aspartate receptor antagonist, may protect from alzheimer disease by blocking the excitotoxic effects of glutamate, independently of the effects of acetylcholinesterase inhibitors.

1.7 What is the prognosis for the patient's daughter?

Onset of the familial form of alzheimer disease, which affects approximately 10% of patients with the disease, is usually 30–60 years of age. Because this patient was older

than 70 years of age at onset, she likely does not have the familial form, and the daughter is unlikely to have an increased risk on the basis of family history alone.

2. A 28-year-old previously healthy woman comes to the physician after suffering loss of vision in her right eye that resolved within a few hours. She also complains of weakness in her legs, urinary incontinence, and difficulty speaking. She has noticed a tremor in her right hand when writing and eating that has worsened over the past few weeks. Although she has had occasional tremors and troubled speech, her problems have never lasted this long and have never been accompanied by urinary incontinence or loss of vision. Upon questioning, she recalls that her mother had similar symptoms when she was young. Physical examination reveals left-sided facial droop, left tongue deviation, and lateral gaze weakness. An MRI is shown in Figure 10-29. Relevant laboratory findings are as follows: White blood cell (WBC) count: 9100/mm3 Hemoglobin: 13.3 g/dL Hematocrit: 37.1% Platelet count: 287,000/mm3 CSF IgG index: 0.89 (normal < 0.66)



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2.1 What is the most likely diagnosis?

Multiple sclerosis (MS). The arrow heads in Figure 10-29 show the lesions of MS.

2.2 What risk factors are associated with this condition?

Risk factors for MS include the following: age 20–50 years (mean age of onset is 30 years). Female gender (female/male ratio is 1.77:1.00). Having grown up in a temperate climate. Family history of MS.

2.3 What anatomic feature could explain the findings on physical examination?

A medial brain stem lesion involving cranial nerves VI, VII, and XII (Figure 1) leads to the constellation of facial droop, tongue deviation, and lateral gaze weakness. the intention tremor indicates cerebellar involvement.

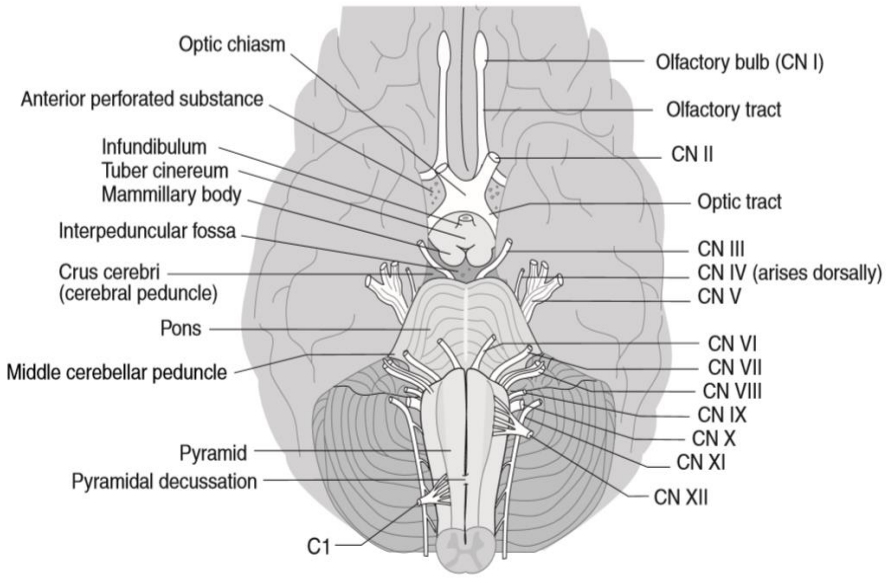

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FIGURE 1. Brain stem anatomy.

2.4 What are the typical CSF findings in this condition?

Oligoclonal bands are seen in 85%–95% of cases. the presence of these immunoglobulins reflects the autoimmune nature of the disease. Oligoclonal bands are not specific to MS and can be elevated in Lyme disease, lupus, syphilis, Sjögren syndrome, and neurosarcoidosis. Similarly, the IgG index is elevated in > 90% of patients with definite MS. the total CSF WBC count is normal in most patients, but an elevated WBC count is nonspecific.

2.5 What is the likely finding on imaging of the brain?

Multiple demyelinating plaques are usually present in the brains of patients with MS, especially in the periventricular region, corpus callosum, and centrum semiovale.

What are the appropriate treatments for this condition? acute attacks are treated with high-dose corticosteroids; however, these drugs do not change the course of the disease. Interferon-β1b is the most common disease-modifying treatment. Supportive care including neurorehabilitation is important in preserving activities of daily living. Interferon-β binds a receptor and induces a transcriptional response that reduces t-cell proliferation and antigen presentation and alters cytokine levels.

3. A 25-year-old woman presents to her physician with difficulty chewing and swallowing food. She also complains of occasional double vision. She states her symptoms are often absent in the morning and appear to worsen as the day progresses.

3.1 What is the most likely diagnosis?

Myasthenia gravis. Differential includes Lambert-Eaton syndrome, which is a paraneoplastic syndrome associated with small cell lung cancer involving muscle weakness; however, strength improves if a contraction is maintained. In myasthenia gravis, symptoms worsen as activity progresses. Lambert-Eaton syndrome also typically spares the extraocular muscles.

3.2 What patient characteristics are typically associated with this diagnosis?
Myasthenia gravis is more commonly seen in women than in men, and most patients are older than 50 years of age when diagnosed.

3.3 What signs and symptoms are commonly associated with this condition?
Patients may present with a variety of findings, including ptosis, diplopia, dysarthria, difficulty chewing, and difficulty swallowing. proximal muscle weakness is usually greater than distal muscle weakness. Weakness increases with use of the muscles.

3.4 What is the pathophysiology of this condition?
Patients develop antibodies against acetylcholine receptors. Because of a higher threshold of activation by acetylcholine, signal transmission across the neuromuscular junction is decreased. this process leads to muscle weakness. the tensilon test assesses the response to edrophonium to distinguish myasthenia gravis from cholinergic crisis; because edrophonium is an anticholinesterase it will improve myasthenia gravis but worsen a cholinergic crisis.

3.5 What tumor is commonly associated with this condition?
Myasthenia gravis has been associated with an increased frequency of thymomas. It is thought that the thymus is the site of production of autoantibodies against acetylcholine receptors. even in patients with no thymus neoplasm, thymectomy has been shown to improve symptoms in 85% of cases.

3.6 What is the appropriate treatment for this condition?
Anticholinesterase drugs are the mainstay of treatment. pyridostigmine is the most common drug prescribed; however, neostigmine may still be used. prophylactic thymectomy is indicated in patients younger than 60 years of age. Corticosteroids and azathioprine are used in refractory cases. plasmapheresis and IVIG can provide temporary relief.

4. A 66-year-old man presents to his physician with a new-onset tremor in his right hand that worsens when he is sitting down watching television. He also experiences difficulty walking, and his friends complain that he has not been able to keep up with them on the golf course. His wife has noticed that he does not seem to get excited about anything.

4.1 What is the most likely diagnosis?
Parkinson disease typically presents with the following symptoms: Tremor that is worse at rest, Rigidity, Akinesia or bradykinesia, and Postural instability (mnemonic: TRAP).

4.2 What are the Parkinson plus syndromes?
The parkinson plus syndromes and their associated symptoms are as follows: dementia with Lewy bodies: fluctuating cognition and visual hallucinations. Multiple system atrophy: autonomic instability. Progressive supranuclear palsy: early postural

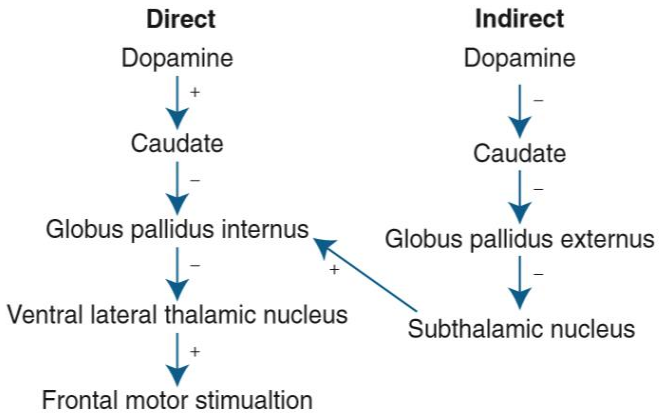
instability, loss of voluntary eye movements, and dysarthria. Corticobasal degeneration: sensory loss, apraxia, aphasia, myoclonus, dementia

4.3 What neuropathologic findings are associated with this condition?

Parkinson disease is marked by significant neuronal loss in the substantia nigra, which decreases dopaminergic input into the basal ganglia. Characteristic findings include depigmentation of neurons in the substantia nigra and concentric eosinophilic cytoplasmic inclusions called Lewy bodies.

4.4 How does a loss of dopamine release from the substantia nigra decrease movement?

Dopamine produced by the substantia nigra activates the direct pathway and inactivates the direct pathway in the basal ganglia. In the direct pathway, dopamine activates the caudate nucleus; this inhibits the globus pallidus internus, which in turn inhibits the ventral lateral thalamus nucleus resulting in frontal motor stimulation. In the indirect pathway, dopamine inhibits the caudate, which inhibits the globus pallidus externus, which in turn inhibits the subthalamic nucleus resulting in stimulation of the globus pallidus internus (the opposite end result as the direct pathway). In both, decreased dopamine results in inhibition of the frontal motor cortex and bradykinesia.



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5. An emergency medical team is called to help a 60-year-old woman with small cell lung cancer who is unconscious at work. Her coworkers state that for about10 seconds before she lost consciousness, she pointed to her right hand as it began twitching rhythmically, then stiffened every muscle and fell down. After about 15 seconds, she became incontinent and her arms and legs began jerking rhythmically. She then was still, unresponsive, and unconscious for about 3 minutes. The medical team notes she is now breathing deeply but remains unresponsive.

5.1 What is the most likely diagnosis?

Seizure. Involvement of the left motor cortex is implicated because the seizure started with right-handed motor activity. In this patient a metastasis is the likely culprit. Seizures can also be caused by infection, ischemia, drug exposure or withdrawal, certain ion imbalances including hypoglycemia and hyponatremia, and trauma.

5.2 How is this condition classified?

This is a simple partial seizure with motor signs secondarily generalizing into a tonic-clonic seizure. During the first 10 seconds, the patient maintained consciousness, pointing to a simple seizure (complex seizures require a loss of consciousness). after the first 10 seconds, her simple partial seizure evolved into a generalized tonic-clonic seizure. the tonic phase is characterized by the immobile contraction of all muscles, and the clonic phase is characterized by the bilateral rhythmic jerking of the extremities.

5.3 Why is the patient breathing deeply after her incident?

The patient is likely responding to acidosis. a respiratory acidosis can develop from the loss of coordinated respirations during the seizure, and a metabolic acidosis can develop as muscles contract under anaerobic conditions and produce lactic acid.

5.4 What is the appropriate treatment for this condition?

Popular antiseizure medications include valproic acid, phenytoin, phenobarbital, primidone, and carbamazepine. Many antiseizure medications work by enhancing γ-aminobutyric acid (GABA) binding on chloride channels. GABA binding allows chloride ions to flow into neurons, thereby inhibiting neuronal firing. Barbiturates act on the same chloride channels and enhance GABA signaling by increasing the duration of chloride channel opening. Benzodiazepines act on the same channels and enhance GaBa signaling, but they do so by increasing the frequency of chloride channel opening.

5.5 What are the most common adverse effects of treatment? Adverse effects of seizure treatments are as follows:

Valproate: hepatotoxicity, neutropenia, thrombocytopenia, teratogenicity (neural tube defects in the fetus). Carbamazepine: hepatotoxicity (check liver function), aplastic anemia, agranulocytosis. Phenytoin: gingival hyperplasia, teratogenicity. Ethosuximide and lamotrigine: Stevens-Johnson syndrome (a bullous form of erythema multiforme that involves mucous membranes and large areas of the body). Carbamazepine and phenobarbital: Induction of cytochrome p450, resulting in drug interactions.

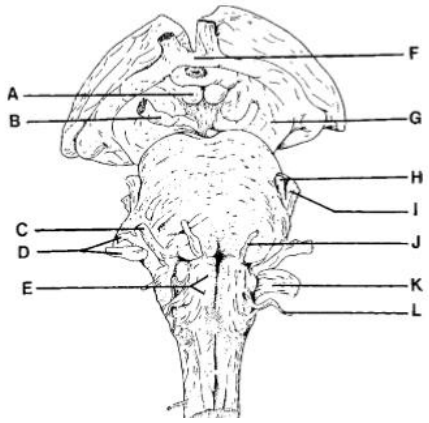
The role of nervous system in regulation of motor function (spinal cord, basal nuclei, cerebral cortex

MCQs STEP 1

1. Emma is a 64-year-old woman who has had heart disease for many years. While carrying chemicals down the stairs of the dry-cleaning shop where she works, she suddenly lost control of her right leg and arm. She fell down the stairs and was able to stand up with some assistance from a coworker. When attempting to walk on her own, she had a very unsteady gait, with a tendency to fall to the right side. Her supervisor asked her if she was all right, and noticed that her speech was very slurred when she tried to answer. He called an ambulance to take her to the nearest hospital. Upon admission, her face appears symmetric, but when asked to protrude her tongue, it deviates toward the left. She is unable to tell if her right toe is moved up or down by the physician when she closes her eyes, and she can't feel the buzz of a tuning fork on her right arm and leg. In addition, her right arm and leg are markedly weak. The physician can find no other abnormalities in the remainder of Emma's general medical examination. Where in the nervous system could a lesion occur that would cause arm and leg weakness but spare the face?

A. Right corticospinal tract in the cervical spinal cord
B. Left inferior frontal lobe
C. Right medullary pyramids
D. Occipital lobe
E. Right side of basilar pons

2. A 28-year-old man was exposed to very cold temperatures for several days and noted sometime afterward that he was unable to smile and display other aspects of facial expression on one side of his face. Which of the following is the affected cranial nerve shown on the illustration below?



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3. A neurological examination of a 75-year-old male revealed that when the abdominal wall was stroked, the muscles of the abdominal wall of the side of the body stimulated failed to contract. Other neurological tests appeared normal. Which of the following is the most likely region of the injury?

A. C1–c5 spinal segments

b. C6–t1 spinal segments

C. T2–t7 spinal segments

D. T8–t12 spinal segments

E. L1–l5 spinal segments

4. A 35-year-old man who had been in good health noticed that his right leg was weak. As the day progressed, he found that he was dragging the leg behind him when he walked, and finally asked a friend to drive him home from work because he was unable to lift his right foot up enough to place it on the gas pedal. He also noticed that his left leg felt a little bit numb. Finally, his wife convinced him to go to the emergency room of his local hospital. In the emergency room, he had a great deal of difficulty walking. He informed the physician that it started slowly several days before but he had ignored the symptoms. His language function, cranial nerves, and motor and sensory examinations of his arms were within normal limits. When the physician examined his right leg, it was markedly weak, with very brisk reflexes in the knee and ankle. Vibration and position sense in the right leg were absent. Pain and temperature testing were normal in the right leg, but these sensations were absent on the left leg and abdomen to the level of his umbilicus. Reflexes in the left leg were normal, but when the physician scratched the lateral portion of the plantar surface on the bottom side of his right foot, the great toe moved up. The remainder of the patient's examination was normal. Which of the following is the primary site of the lesion?

A. Lower brainstem

B. Cervical spinal cord

C. Thoracic spinal cord

D. Lumbar spinal cord

E. Peripheral nerves

5. A patient was diagnosed with a form of motor neuron disease that initially affected neurons situated in the dorsolateral aspect of the ventral horn at L1–L4. Which of the following arrangements best describes the deficit likely to be present?

A. LMN paralysis involving the hand ()

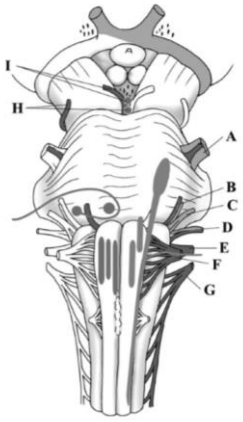
B. UMN paralysis of the upper limb

C. LMN paralysis of the back muscles

D. LMN paralysis of the leg

E. UMN paralysis of the leg

LMN (lower motor neuron)
UMN (upper motor neuron)
6. A 64-year-old male complains of difficulty in swallowing and salivating. The patient also fails to elicit a gag reflex following stroking of the pharynx. Further examination reveals a tumor impinging upon a cranial nerve just beyond its exit from the brain. Which cranial nerve in the figure is affected?



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7. An elderly male suffered a stroke that appeared to involve the left internal capsule rather than the cerebral cortex. It resulted in paralysis of the right arm and leg, the tongue deviated to the right side when he was asked to protrude it; lower (jaw) facial expression on the right side was lost, and his speech was slurred, but fluent and grammatically correct. Which of the following best describes the speech deficit in this patient?
A. Wernicke's aphasia
B. Broca's aphasia
C. Anomia
D. Dysarthria
E. Conduction aphasia
8. A second-year medical student was asked to see a nursing home patient as a requirement for a physical diagnosis course. The patient was a 79-year-old man who was apparently in a coma. The student wasn't certain how to approach this case, so he asked the patient's wife, who was sitting at the bedside, why this patient was in a coma. The wife replied, "Oh, Paul isn't in a coma. But he did have a stroke." Slightly confused, the student leaned over and asked Paul to open his eyes. He opened his eyes immediately. However, when asked to lift his arm or speak, Paul did nothing. The student then asked Paul's wife whether she was certain that his eye opening was not simply a coincidence and whether he really was in a coma, since he was unable to follow any commands. Paul's wife explained that he was unable to move or speak as a result of his stroke. However, she knew that he was awake because he could communicate with her by blinking his eyes. The student appeared rather skeptical, so

Paul's wife asked her husband to blink once for "yes" and twice for "no." She then asked him if he was at home, and he blinked twice. When asked if he was in a nursing home, he blinked once. The student then asked him to move his eyes, and he was able to look in his direction. However, when the student asked him if he could move his arms or legs, he blinked twice. He also blinked twice when asked if he could smile. He did the same when asked if he could feel someone moving his arm. The student thanked Paul and his wife for their time, made notes of his findings, and returned to class. Where in the nervous system could a lesion occur that can cause paralysis of the extremities bilaterally, as well as in the face, but not of the eyes?

A. High cervical spinal cord bilaterally
B. Bilateral thalamus
C. Bilateral basal ganglia
D. Bilateral basilar pons
E. Bilateral frontal lobe

9. You are called to the room of a 93-year-old nursing home patient during morning rounds. She is quite upset because she has awoken with double vision and an inability to open her left eye completely. Your presence calms her down somewhat, and you start asking her questions as you perform a complete cranial nerve exam. Her left eye, under her drooping eyelid, is dilated and rotated down and out. It lacks the normal light reflex when you shine light in either eye. There is no evidence of papilledema in either eye. The rest of the cranial nerve exam is normal. Which of the following is the most likely explanation for this condition?

A. An aneurysm of the left posterior cerebral artery compressing cranial nerve III
B. An aneurysm of the right anterior cerebral artery compressing cranial nerve III
C. A tumor at the left optic canal
D. Glaucoma
E. A left parotid gland tumor compressing cranial nerve VII

10. A 45-year-old woman was brought to her local hospital's emergency room by her husband because of several days of progressive weakness and numbness in her arms and legs. Her symptoms had begun with tingling in her toes, which she assumed to be her feet "falling asleep." However, this feeling did not disappear, and she began to feel numb, first in her toes on both feet, then ascending to her calves and knees. Two days later, she began to feel numb in her fingertips and had difficulty lifting her legs. When she finally was unable to climb the stairs of her house because of her leg weakness, had difficulty gripping the banister, and experienced shortness of breath, her husband urged her to go to the emergency room. The neurologist who examined the patient in the emergency room noticed that she was short of breath while sitting in bed. He asked the respiratory therapist to measure her vital capacity (the greatest volume of air that can be exhaled from the lungs after a maximal inspiration), and the value for this was

far lower than would be expected for her age and weight. Her neurological examination showed that her arms and legs were very weak, so that she had difficulty lifting them against gravity. She was unable to feel a pin or a vibrating tuning fork at all on her legs and below her elbows, but was able to feel the pin on her upper chest. The neurologist could not elicit any reflexes from her ankles or knees. He subsequently advised the emergency room staff that the patient needed to have a spinal tap and be admitted to the intensive care unit immediately. Where in the nervous system was the damage?

A. Frontal lobe
B. Temporal lobe
C. Peripheral nerves and nerve roots
D. Spinal cord
E. Parietal lobe

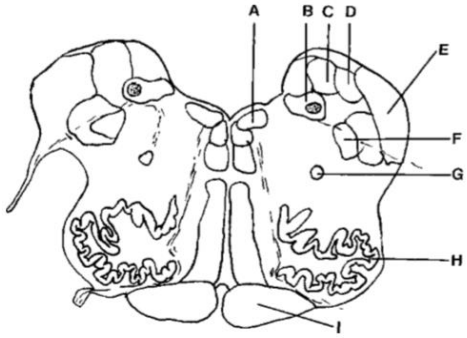
11. In a case involving a patient who experienced hoarseness and dysphagia, it was concluded that the patient suffered from a lesion affecting selective brainstem neurons. Which of the following is the most probable nuclei damaged in this case?

A. Solitary nucleus
B. Deep pontine nuclei
C. Nucleus ambiguus
D. Ventral horn cells of cervical cord
E. Inferior salivatory nuclei

12. A 68-year-old male received a diagnosis of ALS after experiencing weakness in his legs. Over the next year, the disease was progressive and he lost mobility in the use of his arms, legs as well as some cranial nerve functions. Which region or regions of the spinal cord were primarily affected by this disorder?

A. Dorsal horns of the spinal cord
B. Lateral columns of the spinal cord
C. Ventral horns of the spinal cord
D. Dorsal columns and ventral horns of the spinal cord
E. Ventral horns and lateral columns of the spinal cord

13. A young adult male suffers an injury to the region of the face that affects in part the peripheral nerve innervating the tongue, which results in some loss of ability to identify the taste of foods. Which structure in the brainstem would normally receive these peripheral taste inputs?



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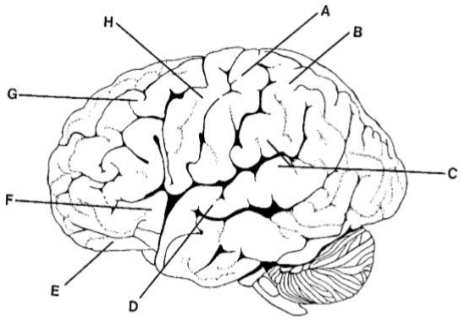
14. A 78-year-old man is found on the ground unconscious one morning and taken to the emergency room of a nearby hospital. After regaining consciousness, he is unable to move his right hand or leg. Which of the regions shown on the illustration was most likely directly affected by the stroke?



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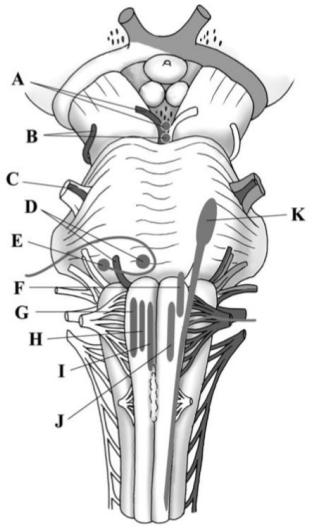
15. Morris is a 79-year-old man who was brought to the emergency room because his family was worried that he suddenly was not using his right arm and leg and seemed to have a simultaneous behavior change. He was unable to write a reminder note to himself, even with his left hand, and he put his shoes on the wrong feet. A neurologist was called to the emergency room to examine the patient. A loud bruit was heard with a stethoscope over the left carotid artery in his neck. When asked to show the neurologist his left hand, he pointed to his right hand, since it could not move. The neurologist asked him to add numbers, and he was unable to do this, despite having spent his life as a bookkeeper. Morris was unable to name the fingers on either hand, and he could not form any semblance of a letter using his left hand. Morris's eyes did not blink when the neurologist waved his hands close to them in the left temporal and right nasal visual fields. The right lower two-thirds of his face drooped. There was some asymmetry of his reflexes between the right and left sides, and there was a positive Babinski's response of his right toe. Where in the CNS is the damage?

A. Right frontal and parietal lobes
B. Left frontal and parietal lobes
C. Right frontal lobe
D. Left frontal lobe
E. Right temporal lobe

16. A 24-year-old male was hiking in the Rockies on a winter day and became lost. He was discovered a day later and was admitted to a local hospital for a precautionary examination. The patient suffered from overexposure to the cold and, when given a neurological test, had difficulty in closing his eye, displayed a loss of both the eye-blink reflex and increased sensitivity to sounds, and had difficulty displaying his teeth and chewing food, especially on the side of the mouth. In addition, his speech was somewhat slurred and he was unable to whistle upon request. Which of the cranial nerves in the following figure was affected by the cold in this individual?



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17. An individual has difficulty adjusting his head, especially after he changes his posture. Which of the following is the most likely pathway affected that might cause this deficit?

A. Lateral vestibulospinal tract
B. Medial vestibulospinal tract
C. Medial reticulospinal tract
D. Lateral reticulospinal tract
E. Rubrospinal tract

18. An elderly male is admitted to the emergency room after having experienced double vision. Further examination reveals the presence of pressure that is exerted upon the wall of the cavernous sinus. When asked by the neurologist to follow the movement of his fingers when they are directed downward in a medial position, the patient is unable to do so with his right eye. Which of the following cranial nerves is affected in this patient?

A. Cranial nerve VIII
B. Cranial nerve VII
C. Cranial nerve VI
D. Cranial nerve IV
E. Cranial nerve III

19. A patient presents in her fifth pregnancy with a history of numbness and tingling in her right thumb and index finger during each of her previous four pregnancies. Currently, the same symptoms are constant, although generally worse in the early morning. Symptoms could be somewhat relieved by vigorous shaking of the wrist. Neurologic examination revealed atrophy and weakness of the abductor pollicis brevis, the opponens pollicis, and the first two lumbrical muscles. Sensation was decreased over the lateral palm and the volar aspect of the first three digits. Numbness and tingling were markedly increased over the first three digits and the lateral palm when the wrist was held in flexion for 30 seconds. The symptoms suggest damage to which of the following?

A. The radial artery

B. The median nerve

C. The ulnar nerve

D. Proper digital nerves

E. The radial nerve

20. A 60-year-old male suffered from excruciating pain on the left side of his face. Since drug therapy was found to be ineffective in alleviating the pain, surgery was indicated. Which of the following structures should be surgically cut or destroyed in order to alleviate the pain?

A. First-order descending sensory fibers contained in the ipsilateral spinal tract of cranial nerve V

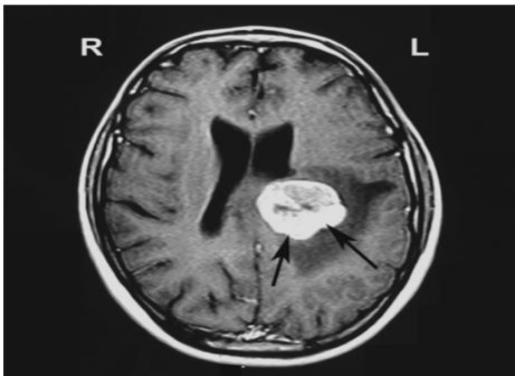
B. Neurons in the ventral posterolateral nucleus of the thalamus

C. Cells contained in the main sensory nucleus of the trigeminal nerve

D. Substantia gelatinosa

E. Midbrain periaqueductal gray

21. A 73-year-old male is admitted to a local hospital after he first began complaining of headaches, which were then followed by a significant weakness in his right arm and leg, slurred speech, and lack of expression on the right side of the jaw. An MRI reveals the presence of a well-defined brain tumor (shown in the following figure). Which of the following structures or regions damaged by. the tumor best accounts for the observed deficits?



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A. Caudate nucleus
B. Globus pallidus
C. Internal capsule
D. Temporal neocortex
E. Dorsal thalamus

22. A patient is admitted to the emergency room after having lost consciousness. Later on, a neurological examination reveals loss of ability to move his right eye laterally when requested to do so. An MRI further reveals the presence of a brainstem infarction. Which of the following is the most likely locus of the infarction?

A. Ventromedial medulla
B. Ventrolateral medulla
C. Dorsolateral pons
D. Dorsomedial pons
E. Dorsomedial midbrain

23. A 46-year-old man found that, over a period of time, he developed progressive bilateral weakness of both upper and lower limbs beginning with the muscles of the hands. However, testing revealed that sensory functions appeared normal. Eventually, this individual was found to have wasting of muscles, fasciculations, and evidence of upper motor neuron (UMN) dysfunction, together with an increase in tendon reflexes. After a few additional months, the patient developed facial weakness and an inability to swallow (dysphagia). Further analysis revealed abnormalities in the electromyegram (EMG) of the upper and lower extremities, denervation atrophy. However, the cerebrospinal fluid (CSF) remained normal. Which of the following is the most likely diagnosis?

A. MS
B. Amyotrophic lateral sclerosis (ALS)
C. Poliomyelitis
D. Myasthenia gravis
E. A cerebral cortical stroke

24. A 24-year-old man who was sitting in a bar found himself in a fight with another slightly intoxicated individual. During the fight, the young man was stabbed in the back. He was taken to the emergency room and following a thorough neurological examination, it was determined that he received a knife wound that destroyed the right half of the spinal cord at the level of the lower cervical cord. Which of the following deficits would most likely result from the knife wound?

A. Impaired bladder functions only
B. Impaired movements of the lower limb only
C. Impaired movements of the upper limb only
D. Loss of sensory functions of the lower limb only
E. Loss of sensory and motor functions of upper and lower limbs

MCQs IFOM

1. A 50-year-old man comes to his primary care provider because of difficulty grasping objects. He has also noticed "worsening depth perception" during the past 3-4 months. He is concerned because a distant relative (his mother's cousin) has Parkinson disease. He has a 30 packyear history of cigarette smoking, but quit 4 years ago. He reports drinking two to three beers per day during the work week and as many as six per day on weekends. On physical examination, he is afebrile and appears anxious. There is a coarse tremor that seems to worsen toward the end of some hand movements, such as when the patient is asked to pick up a pen. He also has difficulty when asked to rapidly alternate tapping the palm of one hand with the finger of another. No nystagmus is noted on ocular examination. Gait and station are normal.
What is the most likely cause of his symptoms?
A. Alcohol intoxication
B. Degeneration of the cerebrocerebellum
C. Degeneration of the spinocerebellum
D. Degeneration of the vestibulocerebellum
E. Wernicke encephalopathy
2. A27-year-old woman with a history of recurrent neurologic complaints presents to her internist's office with a new problem. In the past, she has suffered from temporary loss of vision and bladder incontinence. Last year she felt weakness and loss of sensation in her left leg, which resolved, only to notice similar symptoms in her right arm a few months later. Now she reports that her husband said that her eyes have recently been "moving out of sync" with one another. She admits that at times she has double vision. After a thorough physical exam, the internist suspects that her double vision is due to damage to the left medial longitudinal fasciculus.
A lesion to this area would result in which combination of eye movements ?

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A. Palsy of the left lateral rectus with attempted left lateral gaze
B. Palsy of the left medial rectus with attempted left lateral gaze
C. Palsy of the left medial rectus with attempted right lateral gaze
D. Pasy of the right lateral rectus with attempted right lateral gaze
E. Palsy of the right medial rectus with attempted left lateral gaze
F. Palsy of the right medial rectus with attempted right lateral gaze
3. A 67-year-old man is brought to the emergency department after collapsing at home. He has a history of high cholesterol and hypertension and has smoked cigarettes for the

past 50 years. On arrival, his temperature is 36.1°F (97.4'F), blood pressure is 165/91 mm Hg, and pulse is 96/min. An emergent CT scan of the head shows an ischemic area on the lateral aspect of his left frontal and temporal lobes.
This injury is most likely to produce which of the following symptoms?
A. Ataxia
B. Blindness
C. Expressive aphasia
D. Medial rectus palsy
E. Unilateral leg paralysis
4. A 32-year-old woman with a history of Hashimoto disease comes to her primany care physician because of progressive muscle weakness for the past 6 months. She states that she used to work as yoga teacher but now cannot make it through a class because the repetitive movements become increasingly difficult. The patient also reports that she has lost 10 Ib in the past 6 months because she finds chewing food to be tiring, and describes double vision when trying to read at night. Her only medications include combined oral contraceptives and levothyroxine. She does not smoke or drink alcohol. Her family history is significant for a mother with rheumatoid arthritis. On physical examination, vital signs are normal. Muscles are nontender and deep tendon reflexes are intact. Strength in all four extremities is 5/5 on initial testing but her strength decreases throughout the examination. Thyroid stimulating hormone concentration is within normal limits.
Which of the following is the most likely mechanism of this patient's condition?
A. Antibody-mediated damage to presynaptic cells at the neuromuscular junction
B. Cytotoxic hypersensitivity
C. Delayed (type IV) hypersensitivity reaction
D. Endomysial inflammation with CD8+ cells.
E. Hereditary segmental demyelination of distal nerves
F. Toxin-mediated inhibition of acetylcholine release at the neuromuscular junction
G. Type III hypersensitivity
5. A physician conducts a bedside language examination on an 87-year-old woman who recently had a stroke. The patient's speech is fluent and demonstrates normal intonation and content. She can follow oral commands such as "close your eyes" and "point to the door." However, when asked to repeat individual words or the phrase "no ifs, ands, or buts," she is unable to comply.This patient's stroke most likely damaged which one of the following brain structures?
A. Arcuate fasciculus
B. Broca area in the left hemisphere
C. Broca area in the right hemisphere
D. Medial longitudinal fasciculus

E. Nucleus cuneatus
F. The postcentral gyrus
G. Wernicke area

6. A 64-year-old woman is hospitalized in the intensive care unit after sustaining head trauma during a motor vehicle collision. On arrival, she had a large contusion over her right temporal region but was alert and oriented with no signs of neurological deficit. After 12 hours, she becomes unresponsive to both verbal and physical stimulation. Blood pressure is 170/100 mm Hg, pulse is 50/min, and respiratory rate is 8/min. Physical examination reveals papilledema with a left pupil that is dilated and unreactive to light. Which of the following is the most appropriate next step in treatment?

A. Administer dexamethasone
B. Intubate and hyperventilate
C. Lower the head of the bed 30 degrees
D. Perform lumbar puncture
E. Restrict fluids

7. A 44-year-old woman visits her primary care physician complaining of vision changes. Physical examination reveals the facial and ocular findings shown. The physician decides to perform a series of tests to localize the lesion. First, a drop of cocaine-based solution is applied to both eyes. An hour later, the physician notes the appearance of each eye. The patient returns the following day, and the physician administers a drop of hydroxyamphetamine-based solution to both eyes. An hour later, the physician once again notes the appearance of each eye. Based on the ocular exam, the physician explains that the patient has most likely experienced damage to the postganglionic sympathetic nerves that supply the eye.

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What is the expected response in the affected eye after each eye drop is administered?

A. Constriction with the first drop and no change with the second drop
B. Dilation of the pupil with either drop
C. Dilation with the first drop and no change with the second drop
D. No change in pupil diameter with either drop
E. No change with the first drop and constriction with the second drop
F. No change with the first drop and dilation with the second drop

8. A 45-year-old man comes to the physician because of a 2-week history of lower left back pain that is aggravated by bending or straining and relieved by resting on the right side. Physical examination shows pain on performing a straight-leg raise, and sensory

loss over the back of the left thigh, lateral calf, and lateral foot. There is 3/5 strength in plantar flexion of the left ankle. Which of the following additional physical examination findings is most likely in this patient?

A. Abnormal Achilles (calcaneal) reflex
B. Abnormal patellar reflex
C. Bladder dysfunction
D. Positive Babinski sign
E. Weakness of dorsiflexion

ANWERS MCQs STEP 1

1. The answer is A. Emma had a stroke resulting from occlusion of medial branches of the left vertebral artery, presumably secondary to atherosclerosis (i.e., cholesterol deposits within the artery, which eventually occlude it). The resulting syndrome is called the medial medullary syndrome, because the affected structures are located in the medial portion of the medulla. These structures include the pyramids, the medial lemniscus, the medial longitudinal fasciculus, and the nucleus of the hypoglossal nerve and its outflow tract. Emma's symptoms resulted from damage to the aforementioned structures and may have been caused by the same process (atherosclerosis) that resulted in her heart disease. The weakness of her right side was caused by damage to the medullary pyramid (at the level of the hypoglossal nerve) on the left side. Her face was spared because fibers supplying the face exited above the level of infarct. However, a lesion in the corticospinal tract of the cervical spinal cord above C5 could cause arm and leg weakness and spare the face, because facial fibers exit at the pontine-medulla border. A lesion in the inferior portion of the precentral gyrus of the left frontal lobe would cause right-sided weakness, but would include the face, because this area is represented more inferiorly than are the extremities. Her unsteady gait was a result of the weakness of her right side, but may also have been the result of the loss of position and vibration sense on that side from damage to the medial lemniscus (as demonstrated by the inability to identify the position of her toe with her eyes closed, and the inability to feel the vibrations of a tuning fork). Without position sense, walking becomes unsteady because it is necessary to feel the position of one's feet on the floor during normal gait. Damage to both the medial lemniscus and pyramids at this level causes problems on the contralateral side because this lesion is located rostral to the level where both of these fiber bundles cross to the opposite side of the brain. Damage to the descending component of the MLF could only affect head and neck reflexes, but not gait. Gait is also unaffected by pain inputs. Deviation of the tongue occurs because fibers from the hypoglossal nucleus innervate the genioglossus muscle on the ipsilateral side of the tongue. This muscle normally protrudes the tongue toward the contralateral side. Therefore, if one side is weak, the tongue will deviate toward the side ipsilateral to the lesion when protruded.

2. The answer is C. This figure is a ventral view of the brainstem. Fibers that arise from the dorsal motor nucleus and nucleus ambiguus (in part) exit the brain on the lateral side of the medulla as part of the vagus nerve (K) and innervate the myenteric plexus and smooth muscles of the stomach, which normally function to produce gastric secretions. Cutting some of these fibers would result in a reduction in gastric secretions. The tumor affected the motor component of the trigeminal nerve. (H) The motor root lies medial to the sensory root and innervates the muscles of mastication. The

mammillary bodies (A), which lie on the ventral surface of the brain at the caudal aspect of the hypothalamus, receive many of their inputs from the hippocampal formation and project to the anteroventral thalamic nucleus as the mammillothalamic tract, which in turn send their axons to the cingulate gyrus and then back to the hippocampal formation, forming what is referred to as the Papez circuit. This circuit has been associated with memory functions and the regulation of emotional behavior. The facial nerve (C) exits the brain at the level of the ventrolateral aspect of the caudal pons, and its special visceral efferent component innervates the muscles of facial expression. Damage to this nerve causes loss of facial expression on the side of the face ipsilateral to the affected nerve. The cerebral peduncle (G) is situated in the ventrolateral aspect of the midbrain and contains fibers of cortical origin that project to all levels of the neuraxis of the brainstem and spinal cord. A lesion in this region would affect UMNs that control motor functions associated with both the body and the head region, producing diminution in strength of the muscles of the ipsilateral head and paralysis of the contralateral leg and arm. Note that the selection of choice E, the pyramids, would not have been correct, since the fibers present at this level can only terminate within the medulla or spinal cord, and therefore could not account for the loss of muscle strength associated with the head. First-order somatosensory fibers from the region of the face (I) enter the brain laterally at the level of the middle of the pons as the sensory root of the trigeminal nerve. Damage to this nerve would cause loss of sensation associated with the face. The oculomotor nerve (B) exits the brain at the level of the ventromedial aspect of the midbrain, and some fibers of the general somatic efferent component of this nerve innervate the medial rectus. Damage to this component results in a loss of ability for medial gaze, and the eye will additionally be directed downward because of the unopposed action of cranial nerve IV. Another component of the oculomotor nerve, the general visceral efferent, constitutes the preganglionic parasympathetic neuron in a disynaptic pathway whose postganglionic division innervates the pupillary constrictor muscles. Accordingly, damage to the preganglionic division results in loss of pupillary constriction, which normally occurs in the presence of light as well as in accommodation, and the eye will dilate because of the unopposed action of the sympathetic fibers. The abducens nerve (J) exits the brain at a ventromedial position at the level of the medulla-pontine border, and its fibers innervate the lateral rectus muscle. Damage to this nerve results in a lateral gaze paralysis. The optic chiasm (F) contains fibers that cross over to reach the lateral geniculate nucleus on the side contralateral to the retina from which they originated. Such fibers are associated with the temporal (i.e., lateral) visual fields. Therefore, damage to the optic chiasm will cause blindness in the lateral half of each of the visual fields. Such a deficit is referred to as bitemporal hemianopsia. First-order neurons from the labyrinth organs (D) (i.e., semicircular canals, saccule, and utricle) convey

information concerning the position of the head in space along the vestibular component of the eighth nerve into the central nervous system (CNS). This nerve enters the brain laterally at the level of the upper medulla. Damage to this nerve could result in symptoms such as ringing in the ear, nystagmus, loss of balance, and dizziness. The hypoglossal nerve (L) exits the brain at the level of the middle of the medulla between the pyramid and the olive. These fibers innervate muscles that move the tongue toward the opposite side. For this reason, a lesion of the hypoglossal nucleus or its nerve will result in a deviation of the tongue to the side of the lesion because of the unopposed action of the contralateral hypoglossal nerve, which remains intact.

3. The answer is D. In this case, there is a loss of superficial abdominal reflexes, which require that spinal segments T8–T12 be intact. The test for these reflexes is to stroke a quadrant of the abdominal wall with an object such as a wooden stick. The normal response is for the muscle of the quadrant stimulated to contract and for movement of the umbilicus in the direction of the stimulus.

4. The answer is C. The patient received a diagnosis of Brown-Séquard syndrome, or hemisection of the spinal cord. The lesion is not at the cervical level because motor functions of the upper limbs were considered normal. The examiner can pinpoint the location of the lesion by using the "sensory level," or level at which the loss of pain and temperature begin, by remembering that the lesion affects fibers that have entered the spinal cord one or two levels below it, and then cross to the contralateral side. Therefore, a loss of sensory function at the T10 level indicates a lesion at the T8 or T9 level, a level at which motor deficits may be helpful in diagnosis. In lesions of the thoracic spinal cord, muscles innervated by thoracic nerves are difficult to test. The examiner still expects weakness in the lower extremities, and this helps to make the diagnosis. If the lesion involved the lumbar level, there would be a flaccid paralysis of the lower limb. The disorder could not have been the result of a peripheral nerve injury, because such a possibility could not account for the preservation of pain and temperature in the right leg but with a loss of conscious proprioception associated with that limb. Brown-Séquard syndrome may occur as a result of different types of tumors, infections of the spinal cord, or as a result of a knife or bullet wound.

5. The answer is D. The fact that the disorder affected the neuronal cell bodies of the ventral horn indicates that the patient will present with an LMN paralysis. The affected neurons from L1–L4 innervate the muscles of the lower limb; therefore, the LMN paralysis would affect the leg normally innervated by these neurons.

6. The answer is D. The cranial nerve in question is the glossopharyngeal nerve (cranial nerve IX). As noted in answer to the previous question, the special visceral efferent component supplies the muscles of the pharynx and the general visceral efferent component supplies the parotid gland. Therefore, damage to this nerve would affect swallowing and gag reflex as well as one's ability to salivate. This nerve exits

the brain at the level of the upper medulla in a lateral position just caudal to cranial nerve VIII.

7. The answer is D. Dysarthria is slurred speech, occurring from lesions affecting innervation of the tongue, lips, and palate. We are given evidence that his tongue was weak in that it pointed to the right. The interruption of fibers traveling to the hypoglossal nerve from the left side eventually innervates the right genioglossus muscle, which pulls the tongue to the left. Dysarthria is a motor phenomenon, unlike aphasia, which is a disruption of language. Language is primarily generated in the cerebral cortex; therefore, because the lesion spares the cortex, there were no signs of aphasia.

8. The answer is D. This is an example of the locked-in syndrome, or pseudocoma, caused by an infarction of the basilar pons. Because the tracts mediating movement of the limbs and face run through this region, the patient is unable to move the face, as well as both arms and legs. Consciousness and eye movements are preserved. The pontine basilar pons is supplied mainly by the basilar artery. Complete occlusion of this artery causes deficits on both sides, since this artery supplies both sides of the pons. Sensory loss, including loss of proprioception (feeling the movement of a limb), also occurs as a result of damage to the medial lemniscus bilaterally. This tract contains fibers from the dorsal columns and also runs through the pontine tegmentum. Patients with the locked-in syndrome are often mistaken for comatose patients due to their inability to move or speak. If the lesion spares the reticular formation, an area mediating consciousness in the pons, the patient will remain alert.

9. The answer is A. This condition is most likely due to an aneurysm of the left posterior cerebral artery compressing cranial nerve III. The woman's symptoms, ptosis of the upper eyelid, an eye that is rotated down (because superior oblique muscle, innervated by CN IV is still functioning) and out (because the lateral rectus muscle, innervated by CN VI is still functioning) with a dilated pupil (because sympathetics, which innervate the dilator pupili muscles are still V3 functioning) are all consistent with loss of function of cranial nerve III. An aneurysm in either the posterior cerebral or superior cerebellar artery often can compress cranial nerve III as it exits the midbrain. An aneursym of the right anterior cerebral artery (answer b) would be very unlikely to cause a problem for the left third cranial nerve. A tumor within the left optic canal (answer c) would effect the left optic nerve which passes through it. Cranial nerve III passes into the orbit through the superior orbital fissure along with CN IV, V1, and VI. Neither glaucoma (answer d) nor parotid gland tumor (answer e) would present with those symptoms.

10. The answer is C. This patient does not have a UMN lesion (spinal cord or above) because of the absent reflexes and ascending paralysis bilaterally involving all of the extremities. Lesions in the brain almost always give unilateral findings, and spinal cord

lesions provide clues which identify the distinct level of spinal cord involvement. The damage cannot be in the muscle, because the patient has sensory involvement as well. This case is an example of Guillain-Barré syndrome, or an inflammatory disease of the peripheral nerve resulting from demyelination. Inflammatory cells are found within the nerves, as well as segmental demyelination and some degree of Wallerian degeneration. This damage can cause an ascending paralysis and sensory loss, affecting the arms, face, and legs. The CSF often has a high protein level, making a spinal tap a useful test for the diagnosis of GuillainBarré syndrome. Nerve conduction studies are also helpful in making the diagnosis. Most neurologists believe Guillain-Barré syndrome to be an immunological reaction directed against the peripheral nerve, and some patients have a history of having had some type of infection prior to developing Guillain-Barré syndrome. However, a clear-cut cause is rarely found. Despite a known cause, most patients recover from Guillain-Barré syndrome, although the speed of recovery varies. Treatment is currently available (administration of gamma globulin), and, if instituted early in the course of the disease, decrease in the length of the illness is possible.

11. The answer is C. The axons of the nucleus ambiguus of cranial nerve X innervate the soft palate and pharynx. As noted in Question 204, damage to these neurons would frequently cause dysphagia, hoarseness, and paralysis of the soft palate.

12. The answer is E. In ALS, there is damage initially to ventral horn cells of the spinal cord, producing LMN signs. As the disease progresses, there is involvement of UMNs located in the lateral columns of the spinal cord (i.e., corticospinal dysfunction), thereby producing UMN signs such as an increase in tendon reflexes and the presence of an extensor plantar response. Sensory neurons are not involved in this disorder.

13. The answer is B. Different groups of neurons of the solitary complex (B) respond to taste stimuli and to inputs that signal sudden changes in blood pressure. The medial vestibular nucleus (C) receives direct vestibular inputs from the otolith organ and semicircular canals. Axons of medial vestibular neurons descend to the spinal cord in the MLF and serve to regulate reflexes associated with the head. The inferior vestibular nucleus (D) also receives vestibular inputs, but does not project its axons to the spinal cord. The inferior olivary nucleus (H) receives inputs from the red nucleus and spinal cord, and it projects its axons through the inferior cerebellar peduncle (where it constitutes its largest component) to the contralateral cerebellar cortex, where they synapse with the dendrites of Purkinje cells. The nucleus ambiguus (G) is a special visceral efferent nucleus that is situated in a position ventrolateral to that of the hypoglossal nucleus. Its axons innervate the muscles of the larynx and pharynx and, therefore, are essential for the occurrence of such responses as the gag reflex. The pyramids (I), located on the ventromedial aspect of the brainstem, contain fibers that arise from the sensorimotor cortex. These neurons serve as essential UMNs that

mediate voluntary control of motor functions. The hypoglossal nucleus (A), a general somatic efferent nucleus, is located in the dorsomedial aspect of the medulla. Its axons innervate the muscles of the tongue and cause extrusion of the tongue toward the opposite side, but when this structure is damaged, the tongue protrudes to the side of the lesion when extended. Fibers contained in the inferior cerebellar peduncle (E) comprise the largest single-most input into the cerebellum (approximately 40% of afferents) and these fibers arise from cells located in both the spinal cord and the brainstem.

14. The answer is H. This figure is a lateral view of the cerebral cortex. Cells in the "arm" area of the primary motor cortex (H) project their axons to the cervical level of the spinal cord and are activated at the time when a response of this limb occurs. The leg region of the left primary somatosensory cortex (A) lies immediately caudal to the central sulcus, is almost devoid of pyramidal cells, is referred to as a granulous cortex, and receives inputs from the right leg. Damage to this region would result in loss of vibration sensibility (as well as tactile sensation and two-point discrimination) from the right leg. Damage to the cells situated in the region of the dorsal border of the superior temporal gyrus and the adjoining area of the inferior parietal lobule (Wernicke's area; C) causes impairment in the appreciation of the meanings of written or spoken words. The primary, secondary, and tertiary auditory receiving areas in the cortex are located mainly in the superior temporal gyrus (D). It is the final receiving area for inputs from the medial geniculate nucleus, which represents an important relay in the transmission of auditory signals to the cortex. Damage to this region of the cortex would result in some hearing loss. An additional area of the cortex governing speech (F) is called the motor speech area, or Broca's area. It is situated in the inferior aspect of the frontal lobe immediately rostral and slightly ventral to the precentral gyrus. Lesions of this region produce impairment of the ability to express words in a meaningful way or to use words correctly. The orbital frontal cortex (E) lies in a position inferior and rostral to Broca's motor speech area. This region governs higher-order intellectual functions and some aspects of emotional behavior. Damage to this region often results in personality changes and emotionality. The caudal aspect of the middle frontal gyrus (G) contains cells that, when activated, produce conjugate deviation of the eyes. This action is believed to be accomplished, in part, by virtue of descending projections to the superior colliculus, pretectal region, and horizontal gaze center of the pons. A lesion of this region would result in loss of capacity to produce voluntary horizontal movement of the eyes in one direction. Lesions of the posterior parietal lobe (B) of the nondominant hemisphere will produce a disorder of body image, referred to as sensory neglect. The patient will frequently fail to recognize or neglect to shave or wash those body parts. The patient may even fail to recognize the presence of a hemiparesis involving that part of the body as well. The precentral gyrus

(H) constitutes the primary motor cortex. Lesions of this region produce a UMN paralysis involving a contralateral limb.

15. The answer is B. This case is an example of a lesion of the left (usually dominant) parietal lobe, most often in the angular gyrus, with some involvement of the precentral gyrus in the posterior frontal lobe. There is contralateral UMN weakness (with a positive Babinski's sign), as well as several cortical sensory defects—specifically, right-left confusion, agraphia (inability to write, independent of motor weakness), acalculia (the inability to calculate), and finger agnosia (the inability to designate the fingers). The latter four elements are sometimes referred to as the Gerstmann's syndrome by neurologists, and all represent spatial discriminatory functions of the parietal lobe (often the dominant parietal lobe, which is usually the left). The parietal lobe also subserves other visual-spatial functions such as construction of complex drawings. There are other locations within the CNS where UMN weakness can occur; however, the combination with parietal lobe signs can occur only in this location. If the damage was slightly more extensive, it may have involved Broca's area, causing aphasia.

16. The answer is E. The cranial nerve affected by the cold was the facial nerve (cranial nerve VII). Damage to the facial nerve will produce manifestations of facial paralysis, such as failure to close an eye, loss of the eye-blink reflex, inability to whistle, and difficulty in exposure of the teeth. In this diagram, the facial nerve passes around the dorsal aspect of cranial nerve VI and exits in a lateral position at the level of the lower pons.

17. The answer is B. The medial vestibulospinal tract arises from the medial vestibular nucleus and descends in the MLF to cervical levels, where it controls lower motor neurons (LMNs), which innervate (flexor) muscles controlling the position of the head. The lateral vestibulospinal tract facilitates extensor motor neurons of the limbs, the rubrospinal tract facilitates flexor motor neurons of the limbs, and the reticulospinal tracts modulate muscle tone of the limbs.

18. The answer is D. The trochlear nerve controls downward movement of the eyes when it is situated in a medial position. After exiting the brain, this cranial nerve enters the cavernous sinus (along with cranial nerves III, V, and VI) and enters the orbit through the superior orbital fissure. Therefore, pressure exerted on the cavernous sinus could easily affect the function of this nerve.

19. The answer is B. The patient has a classic case of carpal tunnel syndrome, in which the median nerve is compressed as it passes through the carpal tunnel formed by the flexor retinaculum in the wrist. Evidence for involvement of the median nerve is weakness and atrophy of the thenar muscles (abductor pollicis brevis, opponens pollicis) and lumbricals 1 to 3. Sensory deficits also follow the distribution of the median nerve. The median nerve enters the hand, along with the tendons of the

superficial and deep digital flexors, through a tunnel framed by the carpal bones and the overlying flexor retinaculum. Symptoms are worse in the early morning and in pregnancy because of fluid retention, resulting in swelling that entraps the median nerve. Flexing the wrist for an extended period exaggerates the paresthesia ("Phelan's" sign) by increasing pressure on the median nerve. Neither the ulnar nerve (answer c), radial nerve (answer e), nor radial artery (answer a) passes through the carpal tunnel. The ulnar nerve supplies the third and fourth lumbricals and only the short adductor of the thumb. The radial nerve innervates mostly long and short extensors of the digits and the dorsal aspect of the hand. Proper digital nerves (answer a) lie distal to the carpal tunnel but are only sensory.

20. The answer is A. The spinal trigeminal nucleus receives its sensory inputs from first-order neurons contained in the ipsilateral descending tract of cranial nerve V. A central property of the spinal trigeminal nucleus is that it is uniquely associated with pain inputs (to the exclusion of the main sensory nucleus and mesencephalic nucleus). Fibers from this nucleus mainly project contralaterally to the ventral posteromedial nucleus of the thalamus. Surgical interruption of these descending first-order pain fibers is a practical approach and one that has been carried out by neurosurgeons. Destruction of the ventral posterolateral nucleus would not necessarily destroy the major pain inputs to the cerebral cortex and would additionally be a more difficult structure to destroy surgically. The main sensory nucleus of the trigeminal nerve is not known to convey pain inputs to thalamus and cortex. The substantia gelatinosa conveys pain and temperature sensation from the body and not the head. The midbrain periaqueductal gray constitutes part of a pain-inhibitory system, not one that transmits pain sensations to the cerebral cortex.

21. The answer is C. The deficits observed in this patient were due to damage to the left internal capsule. The tumor impinged upon both genu and posterior limbs of the internal capsule, thus affecting corticospinal and some corticobulbar fibers. Such damage would account for both the contralateral limb paresis (due to damage to the corticospinal tract) and the loss of expression of the contralateral lower jaw (due to damage to corticobulbar fibers that supply the ventral aspect of the facial nucleus, whose axons innervate the lower jaw).

22. The answer is D. The patient was suffering from a lateral gaze paralysis resulting from an infarction of the dorsomedial pons, thus affecting the abducens nerve (cranial nerve VI), whose nucleus is located in the region of the infarction. The fibers of the abducens nerve pass ventrally, exiting the brain in a relatively medial position at the level of the lower pons.

23. The answer is B. ALS is characterized by a progressive loss of motor functions, first seen as weakness in limb muscles, especially those of the fingers, and later of the other limbs. Sensory functions are not affected. Over time, there is wasting, atrophy,

and fasciculations of limb muscles, followed by UMN signs and the patients ultimately die because of respiratory failure or complications of pneumonia. Electromyogram abnormalities can also be observed of the upper and lower extremities. In MS, there is also sensory loss, such as loss or blurring of vision, as well as bladder problems. Poliomyelitis and myasthenia gravis involve LMN symptoms, while a cerebral cortical stroke would result in a UMN disorder without LMN signs.

24. The answer is E. The section depicted in the diagram is taken from the lower cervical cord. The cervical level of the spinal cord can be distinguished from other levels of the cord by the following characteristics: the presence of a well-defined fasciculus cuneatus, situated immediately lateral to the fasciculus gracilis; the presence of well-defined motor nuclei that are clumped into six different groups, three of which can be distinguished; an absence of an intermediolateral cell column; and relatively extensive quantities of both white and gray matter. Thus, a knife wound that destroyed the right half of the spinal cord results in a Brown-Séquard syndrome. The knife wound would cause loss of sensory and motor functions of both upper and lower limbs. The sensory loss of lower limbs would occur because of the damage to ascending fibers from spinothalamic and the fasciculus gracilis (causing loss of pain and temperature of the contralateral side of the body and conscious proprioception of the ipsilateral side), which would also include some loss of these sensations from the upper limb. At the lesion, there is additional loss of these sensations from the upper limb, which enter the cord at this level of spinal cord. Here, there would also be some bilateral pain and temperature loss at the level of the lesion because of the presence of crossing fibers. Because the lesion occurred at the cervical level, it would result in an LMN paralysis of the upper limb and a UMN paralysis involving the lower limb. Klumpke's palsy, a form of brachial plexus palsy, is characterized by weakness of the wrist and finger flexors and of small muscles of the hand, as well as loss of sensation along the medial aspect of the arm.

ANSWERS MCQs IFOM

1. The correct answer is B. The patient presents with numerous issues related to motor coordination, including difficulty grasping objects and rapidly alternating the tapping of one palm with the finger of another. He also has a hand tremor that becomes more noticeable at the end of certain movements. The cerebrocerebellum (or neocerebellum) rests in the lateral cerebellar hemispheres and is responsible for fine movements of the hands and face, motor planning, and coordination of complex tasks. Lesions here usually produce symptoms on the ipsilateral side of the body. Dysdiadochokinesia (the impairment in rapidly alternating hand movements described in the vignette) and intention tremor (also described in the vignette) are common findings in cerebellar

disease. Other symptoms that may be present include dysmetria of hands and arms (past-pointing on finger to nose test), limb ataxia (difficulty with coordinated tasks), and dysarthria (due to oral motor ataxia) that results in scanning speech (slow, slurred, and monotone).

There are many etiologies of cerebellar degeneration that can be divided into acute, subacute, and chronic progressive ataxias. Specific etiologies-including vascular, infectious, autoimmune, paraneoplastic, and genetic causes-can be used to further classify the cerebellar ataxia. Diagnosis and management can be complex and are case specific. In general, neuroimaging, lumbar puncture, and genetic testing are used to guide differential diagnosis and management.

The vestibulocerebellum is located in the flocculonodular lobe of the cerebellum, and is responsible for rapid eye movements, posture, and balance, none of which are abnormal in this patient.

The spinocerebellum (or paleocerebellum) is a midline structure incorporating the anterior vermis of the cerebellum and paravermal parts of the cerebellar hemisphere.

Alcohol intoxication would relapse and remit with ingestion of alcohol and would not get permanently progressively worse.

Spinocerebellar degeneration presents with truncal ataxia.

Thiamine deficiency is common in alcoholics due to poor nutritional intake, and it presents as Wernicke encephalopathy. This condition involves a triad of symptoms: ophthalmoplegia or nystagmus, ataxia, and encephalopathy. This patient does not have the confusion or ocular symptoms associated with Wernicke encephalopathy.

2. The correct answer is C. This patient is a young woman with multiple focal neurologic complaints, separated in time and space, which is most likely indicative of multiple sclerosis. Hemiparesis or hemisensory symptoms, bowel/bladder incontinence, and vision problems are common characteristics. The patient's physician suspects that these new ocular symptoms are due to a lesion in the medial longitudinal fasciculus (MLF), which leads to a condition called internuclear ophthalmoplegia (INO). Normally, the left MLF connects the right nucleus of cranial nerve (CN) VI with the left subnucleus of CN I. Consequently, with right lateral gaze, the right nucleus of CN V sends a signal via the left MLF to the left subnucleus of CN II. This stimulates contraction of the left medial rectus, which preserves conjugate gaze.

In multiple sclerosis, however, demyelination of the left MLF would prevent normal signal transmission, leading to a palsy of the left medial rectus with attempted right lateral gaze and the double vision experienced by the patient. Horizontal nystagmus of the right eye will at so likely be observed. The diagram depicts the signal interruption. A lesion to the right MLF would demonstrate the opposite effect (palsy of the right medial rectus upon attempted left lateral gaze). The palsy does not affect the lateral

rectus muscles, as they lead the movement. The problem lies with the signaling pathway that coordinates the other eye's medial movement.

3. The correct is C. The middle cerebral artery arises from the intemal carotid artery and supplies the lateral aspect of the brain, including the lateral frontal, parietal, and temporal lobes. If the right hemisphere is compromised, you would expect to see left sided weakness and sensory loss, gaze deviation to the right, and neglect of the left visual space. If the left hemisphere is compromised, the findings are similar but on the opposite side. However, since the language centers of the brain are typically in the left hemisphere, issues here often adversely affect speech. Because the middle cerebral artery supplies both the Broca and Wernicke speech areas, an injury to the middle cerebral artery can produce either expressive aphasia (if Broca area is injured) or sensory aphasia (if Wemicke area is injured). Additional impairments may include difficulty with reading, writing, and calculation

The cerebellum is responsible for body positioning, and when damaged, would result in ataxia. The cerebellum is supplied by the superior cerebellar artery, the anterior inferior cerebellar arteries (AlCA), and the posterior inferior cerebellar arteries (PICA). Damage to the ophthalmic artery, a branch of the internal carotid artery, would result in blindness. The anterior cerebral artery provides blood to the portion of the cerebrum responsible for lower extremity sensation and motor.

Unilateral leg paralysis could be the result of an injury to the medial aspect of the motor cortex or to the internal capsule, which are supplied by the antenior cerebral artery and the lateral striate artery, respectively. Though lateral striate arteries are commonly involved in ischemic and hemorrhagic strokes, the internal capsule is also supplied by medial striate arteries.

4. The correct is B. This young woman with a history of autoimmune thyroid disease and progressive weakness, bulbar dysfunction (pain while chewing) and diplopia has a likely diagnosis of Myasthenia gravis (MG), which is caused by a type Il hypersensitivity reaction. Cytotoxic (type l1) hypersensitivity reactions are caused by the action of lgG autoantibodies against cell surface antigens. In the case of MG, autoantibodies are directed against postsynaptic nicotinic acetylcholine (ACh) receptors at the neuromuscular junction (NMJ), leading to complement-mediated injury to the motor endplate. Myasthenia gravis typically manifests in young women in their twenties and thirties and in older men in their sixties through eighties. Symptoms include fluctuating muscle weakness that worsens with use and therefore manifests most severely in the evening. Ocular and bulbar symptoms are also seen. Ocular symptoms include diplopia and ptosis; bulbar symptoms include dysarthria, dysphagia, and difficulty chewing. Although it is no longer performed in clinical practice, improvement of symptoms after the administration of edrophonium (an acetylcholinesterase inhibiton), also referred to as a positive tensilon test, is diagrnostic

of MG. The preferred diagnostic test of choice for the condition is a positive serology for IgG antibodies against acetylcholine receptors. All patients with MG should also be evaluated with chest imaging (either CT or MR) for the presence of a possible thymoma, which is commonly associated with anti-Ach autoantibody formation. In the long term, patients with MG are treated with pyridostigmine, an acetylcholinesterase inhibitor.

Why incorrect answers are wrong:

The presence of autoantibodies to presynaptic voltage-gated calcium channels at the neuromuscular junction is characteristic of Lambert-Eaton syndrome

Toxin-mediated prevention of acetylcholine release at the neuromuscular junction can occur with exposure to botiulinum toxin. Botulism would result in more rapid- onset descending flaccid paralysis and autonomic dysfunction. The disorder is classically associated with the consumption of canned foods.

Delayed (type IV) hypersensitivity reaction against myelin and Schwann cells is characteristic of Guillain-Bàrre syndrome (GBS), which typically occurs after an infection (eg, with Campylobacter jejuni). GBS presents with ascending muscle weakness and decreased-to-absent deep tendon reflexes due to demyelination of spinal motor nerve roots and peripheral nerves.

Type lIl hypersensitivity, as seen in SLE, involves the deposition of immune complexes in unwanted locations and can lead to serum sickness, the arthus reaction, and some symptoms of SLE.

Hereditary segmental demyelination of distal nerves due to Charcot-Marie-Tooth disease can lead to progressive muscle weakness. Pes cavus can be seen on physical exam, as well as legs classically described as being in the shape of inverted champagne bottles due to muscle atrophy. Symptoms are gradual in onset and would be present at a younger age. Ocular and bulbar symptoms are not typical.

Endomysial inflammation with CD8+ T cells leads to skeletal muscle damage characteristic of polymyositis, which presents with progressive, symmetric proximal muscle weakness and tenderness.

5. The correct answer is A. The patient is recovering from a stroke and has normal fluency and comprehension (correctly follows oral commands). However, she is unable to repeat specific words or phrases, which is characteristic of conduction aphasia. This results from a lesion in the arcuate fasciculus, the white-matter tract that connects the Broca area (which lies in the frontal cortex) and the Wernicke area (found in the temporoparietal cortex) in the dominant (usually left) cerebral hemisphere.

If the stroke damaged the other brain structures listed, the expected findings are as follows:

The Broca area is responsible for fluency and production of speech; damage to this area would not allow the patient to speak with the normal rate and tone described in this case.
The medial longitudinal fasciculus is involved in conjugate eye movement and does not affect language. No irregularities regarding bilateral fixation on a single object are noted in the description of this patient.
The nucleus cuneatus is involved in light touch, vibration, and proprioceptive senses, which would be adversely affected by damage. Nothing abnormal regarding these senses was noted during this patient's examination.
The postcentral gyrus is responsible for sensation, which is not impaired in this patient. Damage to the Wernicke area would result in speech that is fluent but empty, meaningless, and full of paraphasic errors. The patient would also have impaired comprehension. None of these language deficits are seen in this patient, who demonstrates only impaired repetition.
6. The correct answer is B. This patient suffered head trauma during a motor vehicle collision and is now comatose, which raises suspicion of elevated intracranial pressure (ICP). She likely suffered an intracranial hemorrhage and is now presenting with all the classic signs of elevated ICP: coma, bradycardia, hypertension, decreased respiratory rate, and papilledema. The changes in vital signs show the characteristic Cushing triad (hypertension, bradycardia, and respiratory depression) in response to the intracranial hypertension. In addition, the dilated and unreactive pupil suggests a possible herniation syndrome. In this situation, the physician should intubate and hyperventilate. This patient should be intubated as soon as possible to protect her airway in case of increased pressure on the brain stem, which can lead to respiratory depression or arrest. In addition, CO, is a powerful vasodilator of cerebral vessels. The use of mechanical hyperventilation to lower partial arterial carbon dioxide pressure to 26-30 mm Hg has been shown to rapidly reduce ICP through vasoconstriction and a decrease in the volume of intracranial blood. A 1-mm Hg change in partial arterial carbon dioxide pressure is associated with a 3% change in cerebral blood flow. The effect of hyperventilation on ICP is short-lived, however, and is primarily used to buy time to identify and treat the underlying cause of elevated ICP. Other therapies for acute increases in ICP are the use of osmotic diuretics, such as mannitol. However, these are only temporizing measures. In a patient with such a poor clinical presentation, emergent surgical decompression is the definitive treatment. Lowering of the head of the bed will restrict blood flow exiting the brain, creating an elevation in the intracranial pressure which would exacerbate this patient's symptoms. A lumbar puncture may rapidly relieve intracranial pressure, but this can cause decompression of the brain structures and worsen herniation.mFluid restriction is not necessary in patients with elevated ICP due to compensatory vasodilation and worsening of the elevation in ICP.

Glucocorticoids like dexamethasone are no longer recommended in the treatment of elevated ICP due to traumatic head injury.

7. The correct answer is D. The patient presents with left-sided ptosis (drooping eyelid) and miosis (constricted pupil) on her initial physical exam, which are findings consistent with Horner syndrome. Anhidrosis (absence of sweating) is the third classic symptom, although it is difficult to discern in a patient at rest. Horner syndrome can be caused by a lesion anywhere along the sympathetic pathway to the eye and face (see diagram). Based on the test results, the physician diagnosed this patient with damage to the sympathetic postganglionic neuron. A lesion in this location results in no stimulation of the long ciliary nerve. This in turn causes a lack of stimulation of the iris dilator pupillae muscle, rendering the pupil completely unable to dilate. The unopposed action of the parasympathetically innervated pupillary constrictor muscle results in a chronic miosis.mThe cocaine-based drop, which inhibits the reuptake of norepinephrine, should cause mydriasis (pupillary dilation) in an eye with normal sympathetic function. However, a pupil lacking intact sympathetic innervation due to a lesion of the postganglionic neuron anywhere along the pathway would not react, due to the absence of endogenous norepinephrine in the neuromuscular synapse. The second drop, hydroxyamphetamine, causes the release of stored endogenous norepinephrine at the neuromuscular synapse. In a normal eye with intact sympathetic innervation, this drug, like cocaine, would cause pupillary dilation. If Horner syndrome is caused by a CNS lesion, then the eye can still dilate in response to amphetamine by releasing stored norepinephrine from the postganglionic neuron that innervates the iridial dilator muscle. In contrast, a lesion of the postganglionic neurons (and accompanying degeneration of the neuromuscular synapses) will produce an iis that is unresponsive to either drug. However, a lesion of the sympathetic postganglionic neuron will result in less dilation of the affected eye than in a normal pupil.

8. The correct answer is A. The patient presents with sensory loss over the back of the thigh, which correlates with the distribution of the S1 and S2 dermatomes (see image). Weakness in plantar flexion at the ankle indicates a problem with the posterior compartment of the leg (gastrocnemius, soleus, plantaris, popliteus, tibialis posterior, flexor digitorum longus and flexor hallucis longus, which is innervated by the tibial nerve (L4-52). These findings are consistent with an L5-S1 disc herniation causing an S1 radiculopathy. Note that the L5 nerve root that exits between L5 and S1 is spared while S1 and possibly S2 are affected. L5-S1 is the second most common location for disc herniation after L4-L5. These patients can also demonstrate loss of the Achilles (calcaneal) reflex, which is a test of the S1 root and the gastrocnemius, soleus, and plantaris muscles. Patients will therefore present with weakness of plantar flexion and difficulty with toe-walking. The sciatic nerve is formed by the sacral plexus; several nerve roots unite to form a single nerve near the piriformis muscle. ‘Sciatica" and disc

herniation are often incorrectly used interchangeably, but they are not synonymous. Sciatic nerve iritation can produce similar findings, but patients with sciatic nerve irritation do not have low back pain. Some causes of sciatic nerve irritation include sacroiliac joint dysfunction, a tight piriformis muscle, and an aberrant exit of the sciatic nerve through the belly of the piriformis muscde (ocuring in 206 of the population). The presence of low back pain is key to differentiating sciatic-t ype symptoms that are caused by disc herniation from sciatic nerve irritation alone. Herniation affecting the L4 nerve root can cause an abnormal patellar reflex. A lesion in the corticospinal tract can a positive Babinski sign. Damage to the distal spinal cord (conus medullaris) can cause bladder dysfunction. L4-L5 disc disease may cause difficulty in dorsiflexion.

CLINICAL CASES

1. A 35-year-old construction worker is taken to the emergency department (ED) after an accident in which a piece of metal became lodged in his back. The patient has excruciating pain at the site of his injury and is unable to move his right leg. In the ED, neurologic examination reveals paralysis of the right leg, ipsilateral hyperactive patellar reflex, and a positive Babinski sign. The patient can move his left leg without difficulty and has a normal patellar reflex and no Babinski sign. However, sensory testing reveals loss of temperature and pinprick sensation on the left leg up to the navel and loss of vibration sensation on the right leg up to the navel.

1.1 What is the most likely diagnosis? Brown-Séquard syndrome due to a hemicord lesion. Brown-Séquard syndrome is characterized by ipsilateral spastic (upper motor neuron type) paralysis (1 in Figure 10-2), ipsilateral loss of vibration and position sensation (2 in Figure 10-2), and contralateral loss of pain and temperature sensation (3 in Figure 10-2).

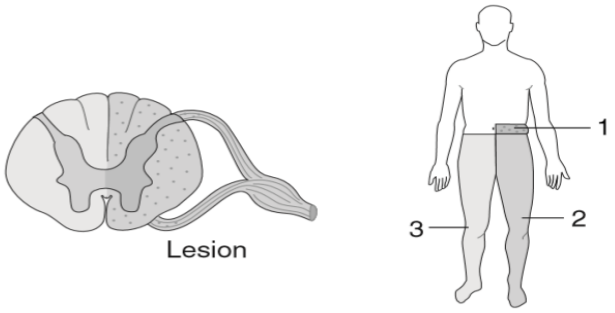

FIGURE 10-2. Brown-Séquard syndrome. (Repro-

Reproduced from First aid cases for USMLE STEP 1

1.2 At what level is the lesion located?

The loss of sensation up to the navel suggests that the lesion is near Th10, because the dermatome that includes the navel is supplied by Th10.

1.3 Damage to which tracts is causing the ipsilateral deficits in this case?

The motor deficits are due to damage to the lateral corticospinal tract (Figure 10-3), which carries motor neurons from the cortex that have decussated in the pyramids. the loss of vibration and position sense is due to damage to the dorsal columns, which carry information from sensory nerves that enter through the dorsal root, ascend to the caudal medulla (where the primary neuron synapses), and then cross to ascend to the contralateral sensory cortex. these deficits are ipsilateral because the tracts cross the midline high in the spinal cord.

1.4 Damage to which tracts is causing the contralateral deficits in this case?

The loss of pain and temperature sensation is due to damage to the spinothalamic tract (Figure 10-3). the sensory neurons that travel in the anterolateral tract enter the spinal cord through the dorsal root, synapse almost immediately, and cross the midline (within one or two levels) via the anterior commissure to ascend to the cortex.

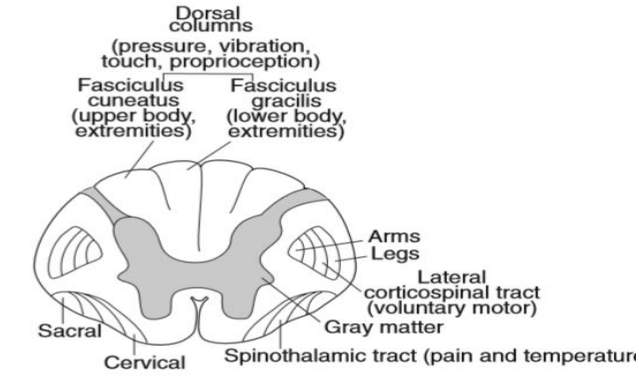

FIGURE 10-3. Spinal cord and associated tracts.

Reproduced from First aid cases for USMLE STEP 1

1.5 If the lesion were above T1, how would the presentation differ?

A hemicord lesion above t1, in addition to the findings above, will present as Horner syndrome, which consists of ptosis, miosis, and anhidrosis (droopy eyelid, constricted pupil, and decreased sweating).

2. A 38-year-old man presents to his primary care physician with a complaint of progressive weakness in his hands and feet. The patient states that these symptoms have slowly progressed over the past few months. Initially, he was unable to manipulate small objects such as picking up a coin or buttoning his shirt. Now he complains of difficulty grasping a gallon of milk and notices the muscles in his hands twitching. He often trips while walking because he feels he cannot lift his toes up and lacks coordination. In addition, he says that the muscles in his leg occasionally cramp or spasm.

2.1 What is the most likely diagnosis?

Amyotrophic lateral sclerosis (ALS), or Lou Gehrig disease, is a neurodegenerative disorder that causes progressive muscle weakness. there are several aLS variants classified on the basis of their pattern of distribution. progressive bulbar palsy affects the motor nuclei of cranial nerves, and pseudobulbar palsy describes any condition that causes bilateral corticobulbar disease. progressive spinal muscular atrophy is a lower motor neuron deficit involving anterior horn cells of the spinal cord. primary lateral sclerosis predominantly affects the upper motor neurons.

2.2 Where are the lesions located and how does this explain the hallmark findings?

The hallmark of this disorder is the presence of both upper motor neuron (UMN) and lower motor neuron (LMN) lesions. aLS affects anterior horn motor neurons in the spinal cord (LMN) and the lateral corticospinal tracts carrying UMNs from the cortex. Sensory and cognitive functions are generally preserved.

2.3 How is this condition distinguished from the ascending paralysis syndromes?

ALS has both UMN and LMN findings whereas Guillain Barré syndrome (or acute inflammatory demyelinating polyradiculoneuropathy) and chronic inflammatory

demyelinating polyradiculoneuropathy are solely LMN diseases and present with characteristic decreased reflex response.

2.4 What distinguishes UMN signs from LMN signs?

UMN signs include hyperreflexivity, increased tone, positive Babinski sign, and muscle spasm. LMN signs include weakness, muscle atrophy, and muscle fasciculations.

2.5 What is the course of this disease?

ALS is currently an untreatable disease with progressive neurodegeneration and muscle weakness, resulting in death within 3–5 years of diagnosis. riluzole can prolong survival by 2–3 months, likely by blocking glutamatergic transmission in the central nervous system (CNS). Supportive care, including dietary modification, respiratory assistance, and palliative care, is an important part of management. Neuromuscular respiratory failure is the primary cause of death.

3. A 70-year-old man with a history of rheumatoid arthritis comes to his physician complaining of weakness 1 day after a motor vehicle accident. Physical examination reveals intact sensation and strength in the lower extremities but weakness in the upper extremities bilaterally. The patient is able to move his arms parallel to the ground but is unable to lift his arms, forearms, or hands upward against gravity. Strength is rated 2/5. CT scan of the cervical spine rules out cervical spine fracture, and MRI demonstrates traumatic C6 disk herniation, buckling of the ligamentum flavum, and edema within the cervical cord in that area.

3.1 What is the most likely diagnosis?

Central cord syndrome. this syndrome is characterized by upper extremity weakness that exceeds lower extremity weakness and varying degrees of sensory loss below the level of the lesion.

3.2 What is the arterial supply to the cervical spinal cord?

The spinal cord is supplied by an anterior spinal artery (which is supplied by the vertebral arteries) that supplies the anterior two-thirds of the cord and by two posterior spinal arteries (which are supplied by the vertebral posterior inferior cerebellar arteries) that supply the dorsal columns and part of the posterior horns.

3.3 What is a vascular watershed zone?

A watershed zone is an area between two major arteries in which small branches of the arteries form anastomoses. Important watershed zones lie between the cerebral arteries (eg, middle and anterior cerebral arteries) and in the central spinal cord. these areas are susceptible to infarction during hypotension or hypoperfusion. In this case, edema and trauma impair blood flow to the cervical cord, and the predominant symptoms result from damage within the central cord watershed zone.

3.4 What is supplied by the long tracts in the areas labeled “Region A” in Figure 10-5?

Region a in Figure 10-5 indicates the most medial portions of the corticospinal tracts. these fibers supply the muscles of the upper extremity. Because they are medial structures, motor impairment of the upper extremities can occur after a smaller central cord lesion. the cross-hatched pattern in Figure 10-6 indicates the area of impairment that is associated with a central cord lesion.

3.5 What changes in the biceps, triceps, and brachioradialis reflexes are expected after damage to the anterior horn cells supplying the C6 nerve root?

The biceps reflex, which is regulated by fibers from C5 and C6, will be moderately diminished secondary to diminished lower motor neuron input. the triceps reflex is regulated primarily by C7 and should thus be unaffected by a C6 lesion. the brachioradialis reflex is primarily regulated by C6 and will thus be markedly diminished after a C6 lesion.

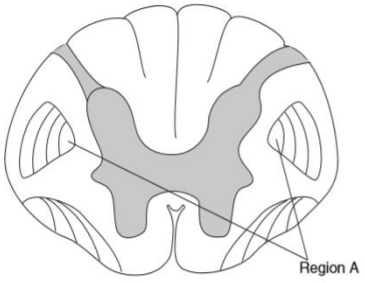

FIGURE 10-5. **Axial view of the spinal cord, showing the most medial portions of the corticospinal tracts (region A).** (Reproduced, with permission, from Le T, et al. *First Aid for the USMLE Step 1: 2008*. New York: McGraw-Hill, 2008: 371.)

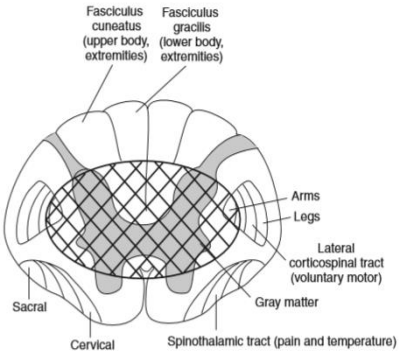

FIGURE 10-6. **Axial view of the spinal cord, showing the area of impairment associated with a central cord lesion.** (Reproduced, with permission, from Le T, et al. *First Aid for the USMLE Step 1: 2008*. New York: McGraw-Hill, 2008: 371.)

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4. A 45-year-old woman presents to her physician with a 3-month history of anxiety, tremor, hyperreflexia, hair thinning, and an unintentional weight loss of 4.5 kg (10 lb). She is treated surgically. After surgery, her symptoms have resolved, but the patient now complains of hoarseness.

4.1 What is the cause of the patient's hoarseness?

This patient underwent surgery for hyperthyroidism. Damage to the recurrent laryngeal nerve may occur as the surgeon is ligating the inferior thyroid artery, which is adjacent to the nerve.

4.2 What cranial nerve is involved in this patient?

The recurrent laryngeal nerve is a branch of the vagus nerve (CN X).

4.3 This nerve provides motor innervation to which structures?

The recurrent laryngeal nerve innervates all intrinsic muscles of the larynx except for the cricothyroid, which is innervated by the external laryngeal nerve (also a branch of CN X).

4.4 What is the course of this nerve?

The left recurrent laryngeal nerve branches off the vagus nerve at the level of the aortic arch, wraps posteriorly around the aorta, and ascends superiorly to the larynx (Figure 10-8). the right recurrent laryngeal nerve branches off the vagus at the level of the right subclavian artery and vein and wraps around the artery to ascend posteriorly to the larynx. Because the left recurrent laryngeal nerve has a long course arising from the vagus in the superior mediastinum, it is prone to injury from abnormal structures, such as enlarged lymph nodes, aneurysm of the arch of the aorta, a retrosternal goiter, or a thymoma.

4.5 What other structures can be damaged during this surgery?

Surgical technique focuses on preservation of the parathyroid glands, and hypoparathyroidism can occur after surgery. For this reason surgeons often remove the parathyroid gland and reimplant it elsewhere in the neck.

4.6 What are other scenarios in which this nerve may be injured?

Left atrial enlargement (eg, from mitral regurgitation) and tumor in the apex of the right upper lobe of the lung can impinge on and injure the recurrent laryngeal nerve. Injury of the left recurrent laryngeal nerve may also result in compression by abnormal structures in the superior mediastinum, as described above.

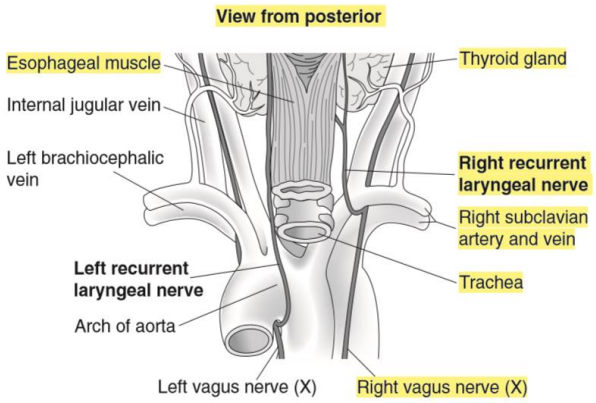

FIGURE 10-8. Course of the recurrent laryngeal nerve. (Reproduced, with permission, from Bhushan V, et al. *First Aid for the USMLE Step 1: 2005.* New York: McGraw-Hill, 2005: 83.)

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5. A 27-year-old man comes to his physician complaining of a tingling sensation in his toes and progressive weakness in both legs. On questioning, he says that he had bloody diarrhea, nausea, vomiting, and cramps 3 weeks ago that lasted for a few days. He has not traveled recently and has not eaten anything out of the ordinary. Physical examination reveals markedly decreased patellar and Achilles tendon reflexes bilaterally.

5.1 What is the most likely diagnosis?

Guillain-Barré syndrome (GBS), or acute inflammatory demyelinating polyradiculoneuropathy, is characterized by symmetric ascending muscle weakness or paralysis that begins in the lower extremities. hyporeflexia or areflexia is invariable but may not be present early in the course of disease.

5.2 What physical findings are commonly associated with this condition?

Findings in GBS include ascending paresthesias, cranial nerve deficits leading to dysphagia, dysarthria, facial weakness, papilledema, autonomic dysfunction, and respiratory muscle paralysis in extreme cases. Figure 10-12 shows papilledema of the optic nerve head in GBS, along with the vascular congestion, elevation of the nerve head, and blurred disc margins often seen in papilledema, papillitis, and compressive lesions of the optic nerve.

5.3 In what settings does this condition usually occur?

GBS often occurs 1–3 weeks after a gastrointestinal or upper respiratory tract infection, vaccination, or allergic reaction. Common associated infections include Campylobacter jejuni and herpesvirus. although a preceding event is present in most patients, approximately one third of patients with GBS report no such events during the preceding 1–4 weeks.

5.4 What is the etiology of this condition?

GBS is thought to be an autoimmune reaction that develops in response to a previous infection or other medical condition. this process results in aberrant demyelination of peripheral nerves and ventral motor nerve roots. Cranial nerve roots can also be affected.

5.5 What laboratory finding is likely in this condition?

Cerebrospinal fluid (CSF) reveals a markedly elevated protein concentration with a normal cell count, commonly referred to as albuminocytologic dissociation. this contrasts the increased cell counts typical of CNS infection. Increased CSF protein can lead to papilledema.

5.6 What is the appropriate treatment for this condition?

The first element of GBS management is supportive care and treatment of the underlying condition with either IVIG antibody or plasmapheresis. pulmonary function should be monitored with peak flow studies to assess for respiratory failure. rehabilitation may be required to restore function.

5.7 If this patient’s symptoms worsen over the next few months with no signs of improvement, what alternative diagnosis should be considered?

Chronic inflammatory demyelinating polyradiculopathy is a chronic, progressive, or chronic progressive counterpart of GBS that often presents with similar symptoms.

6. A 39-year-old man is concerned about his health because his father died at 45 years of age after several years of dementia, uncontrollable twitching, and dance-like movements in his extremities. On further questioning, the patient reports that many members of his family have had similar symptoms.

6.1 What condition is the patient at risk for developing?

Huntington disease is characterized by dementia, choreoathetoid movements of the face and extremities, and early death. huntington disease has an autosomal dominant

inheritance. Other causes of early-onset dementia include early-onset alzheimer disease, multiple sclerosis, hIV infection, or Creutzfeldt-Jakob disease (much rarer).

6.2 What is the genetic basis of this condition?

A mutation in chromosome 4 results in expansion of trinucleotide CaG repeats, which may decrease transcription of a striatal neurotrophic factor (brain-derived neurotrophic factor).

6.3 What neuronal pathology in patients with this condition makes CT imaging useful?

Patients with Huntington disease have marked atrophy of the striatum, including the caudate and putamen, representing degeneration and loss of γ-aminobutyric acid–ergic and cholinergic neurons.

6.4 What other conditions often present with similar movement abnormalities?

Sydenham chorea in rheumatic fever, tardive dyskinesia, and Wilson disease are among other diseases associated with choreoathetoid movements.

6.5 What is the prognosis for this patient?

Expansion of trinucleotide repeats over successive generations leads to earlier manifestations of disease in offspring; this is called anticipation. the patient's father died at age 45 years and likely developed huntington disease many years earlier. If this patient had the genetic mutation, he might already be expected to show symptoms.

6.6 What other conditions are associated with trinucleotide repeats?

Fragile X syndrome, myotonic dystrophy, and spinocerebellar ataxia types I and II are also associated with trinucleotide repeats.

7. A 72-year-old woman is at home with her husband when he notices she sounds confused even though she had been speaking clearly just moments before. He brings her into the emergency department, where she is unable to follow commands. Her speech is fluent but does not make any sense. CT scan of the head is shown in Figure 10-35.

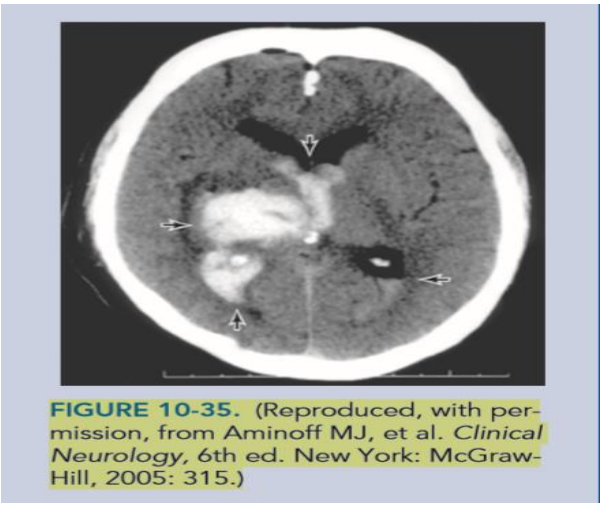


FIGURE 10-35. (Reproduced, with permission, from Aminoff MJ, et al. *Clinical Neurology*, 6th ed. New York: McGraw-Hill, 2005: 315.)

Reproduced from First aid cases for USMLE STEP 1

What is the most likely diagnosis?

Stroke. Figure 10-35 shows extensive hemorrhage in the thalamus (left arrow) and its extension into the third (top arrow), ipsilateral (bottom arrow), and lateral (right arrow) ventricles.

7.1 What risk factors are associated with this condition?

Advanced age. Cardiovascular disease. Carotid disease. Diabetes mellitus. Dyslipidemia. Family or personal history of transient ischemic attack or stroke. hypertension. Smoking.

7.2 What type of aphasia does the patient exhibit?

The combination of fluent but nonsensical speech and poor comprehension is characteristic of Wernicke aphasia (sensory aphasia). these patients also display poor repetition and naming ability. Other findings commonly associated with Wernicke aphasia include contralateral visual field cut (due to ischemia of optic radiation) and anosognosia (unawareness of one's deficit).

7.3 A lesion in what anatomic area causes these findings?

Wernicke aphasia is usually the result of ischemia in the superior temporal gyrus, which is supplied by the inferior division of the left middle cerebral artery.

7.4 What speech pattern results when this condition affects the inferior frontal gyrus?

The inferior frontal gyrus controls motor aspects of speech. a stroke in this area causes Broca aphasia (motor aphasia), which is characterized by nonfluent, agrammatic speech. Because of the proximity of the primary motor cortex for the face and arm, dysarthria (difficulty in articulating words) and right face and arm weakness are often associated with Broca aphasia. Comprehension is intact in these patients.

7.5 If the patient had nail-bed hemorrhages, nodules on her fingers and toes, and retinal hemorrhages, what diagnosis should be considered?

This constellation of symptoms suggests infective endocarditis, which is characterized by splinter hemorrhages, Osler nodes on the pads of the fingers and toes, and roth spots on the retina. Infective endocarditis can lead to the release of thrombi from the valvular vegetations, resulting in embolic events.

The sensory function of the nervous system
MCQs STEP 1

1. Following hemisection of the spinal cord at the level of approximately T3, a patient experiences loss of pain and temperature on the left side of the leg. Which of the following tracts was affected by the hemisection of the cord that could account for this deficit?

A. Right fasciculus cuneatus
B. Right fasciculus gracilis
C. Right spinothalamic tract
D. Left spinothalamic tract
E. Left corticospinal tract

2. A 17-year-old boy is admitted to the hospital with a traumatic brain injury, sustained when he fell off his motorcycle. He develops a fever of 39°C, which is unrelated to an infection or inflammation. The fever is most likely due to a lesion of which of the following?

A. The lateral hypothalamus
B. The arcuate nucleus
C. The posterior nucleus
D. The paraventricular nucleus
E. The anterior hypothalamus

3. A 34-year-old woman, who has been immobilized with a sprained ankle for the past 4 days, develops a throbbing pain that has spread to her entire left leg. History reveals that she has been taking oral contraceptives for 15 years. Compared to localized pain, such as one might experience from a needle stick, which of the following is true of ischemic pain?

A. Ischemic pain sensory fibers are classified as A delta (Ad) sensory fibers.
B. Ischemic pain is produced by overstimulating somatic touch receptors.
C. Ischemic pain is transmitted to the brain through the neospinothalamic tract.
D. Ischemic pain receptors quickly adapt to a painful stimulus.
E. Ischemic pain sensory fibers terminate within the substantia gelatinosa of the spinal cord.

4. A patient in the emergency department requires suturing of a deep 2-cm laceration. To reduce discomfort we first infiltrate the surrounding area with lidocaine. Which of the following functions or sensations is most likely to disappear first as the drug's effects build up, and the last to reappear as the drug's effects wear off?

A. Autonomic efferent function
B. Motor nerve activity
C. Pain
D. Pressure (deep or heavy pressure)

E. Temperature

5. A 42-year-old female complained about a painful and burning sensation in both hands and arms. Following a neurological examination, it was determined that the patient was suffering from a peripheral neuropathy caused by a virus that selectively attacked sensory fibers in the arms mediating pain and temperature signals. Concerning the distribution and sites of termination of these sensory fibers in the central nervous system (CNS), their sites of termination include which of the following regions?

A. Laminas I and II of the gray matter of the spinal cord ipsilateral to their site of entry into the cord

B. Laminas III and IV of the gray matter of the spinal cord contralateral to their site of entry into the cord

C. Laminas VIII and IX of the gray matter of the spinal cord ipsilateral to their site of entry into the cord

D. Laminas VIII and IX of the gray matter of the spinal cord contralateral to their site of entry into the cord

E. Lower brainstem nuclei ipsilateral to their site of entry into the cord

6. A 55-year-old woman undergoes surgery. She receives several drugs for preanesthesia care, intubation, and intraoperative skeletal muscle paralysis; and a mixture of inhaled anesthetics to complete the balanced anesthesia. Toward the end of the procedure she develops hyperthermia, hypertension, hyperkalemia, tachycardia, muscle rigidity, and metabolic acidosis. Which of the following drugs is most likely to have participated in this reaction?

A. Fentanyl

B. Halothane

C. Ketamine

D. Midazolam

E. Propofol

MCQs IFOM

1. A 73-year-old male is admitted to the hospital to undergo correction of an abdominal aortic aneurysm after having back, lank, and abdominal pain over the past few weeks. There was significant blood loss during his surgery and he received 3 units of packed RBCs intraoperatively.lin the recovery room, the patient has paralysis and abnormal sensation in his lower extremities. On evaluation, lower extremity deep tendon reflexes are absent. Laboratory studies show:

WBC count: 4000/mm3

Hematocrit: 28%

Hemoglobin: 8.3 g/dL

Platelet count: 344,000/mm

Nat: 143 mEg/L
K:4.4 mEq/L
CIr: 103 mEq/L
Blood urea nitrogen: 20 mg/dL
Creatinine: 1.1 mg/dL
Mean corpuscular volume: 85 fL
Which of the following would most likely be observed on sensory examination of the lower extremities?
A. Decreased pain sensation; decreased vibration sense
B. Decreased pain sensation; normal vibration sense
C. Decreased strength; normal pain sensation
D. Normal pain sensation; decreased vibration sense
E. Normal strength; decreased pain sensation
2. A 26-year-old man is brought to the emergency department after being found unresponsive in his apartment by a friend three hours earlier. He has no known medical conditions and does not take any medications. On exam, his temperature is 37.1C (98.7° F), blood pressure is 110/89 mm Hg, pulse is 55/min, and respirations are 8/min. The patient's pupils are 2 mm in size and do not appear to constrict with light. His heart rate is regular and lungs are clear to auscultation bilaterally. There are needle tracks on his arm.
Which of the following is most likely responsible for this patient's respiratory depression?
A. Activation of K receptors
B. Activation of μ receptors
C. Activation of GABA receptor
D. Blockade of norepinephrine reuptake
E. Inhibition of GABA receptor
F. Inhibition of muscarinic receptor

ANSWERS MCQs STEP 1

1. The answer is C. The spinothalamic tract carries fibers mediating pain and temperature. The primary pain fibers enter the spinal cord and pass one or two segments in Lissauer's marginal zone before making a synapse with neurons that form the lateral spinothalamic tract. Fibers of the lateral spinothalamic tract then cross to the contralateral side one or two segments above or before where the primary afferent fibers have entered the cord. Accordingly, pain and temperature are lost below the lesion on the contralateral side. The cuneate and gracile fasciculi mediate proprioception and vibration in association with the same side of the body from which these fibers originate, and the corticospinal tract mediates voluntary motor function.

2. **The answer is E.** The hypothalamus regulates body temperature. Core body temperature, the temperature of the deep tissues of the body, is detected by thermoreceptors located within the anterior hypothalamus. The anterior hypothalamus also contains neurons responsible for initiating reflexes, such as vasodilation and sweating, which are designed to reduce body temperature. Heat-producing reflexes, such as shivering, and heat-maintenance reflexes, such as vasoconstriction, are initiated by neurons located within the posterior hypothalamus.

3. **The answer is E.** Activating nociceptors on the free nerve endings of C fibers produces ischemic pain. The C fibers synapse on interneurons located within the substantia gelatinosa (laminas II and III) of the dorsal horn of the spinal cord. The pathway conveying ischemic pain to the brain is called the paleospinothalamic system. In contrast, well-localized pain sensations are carried within the neospinothalamic tract. Ischemic pain does not adapt to prolonged stimulation. Pain is produced by specific nociceptors and not by intense stimulation of other mechanical, thermal, or chemical receptors.

4. The answer is C. For the key to the simple answer, consider the British term for local anesthetics: regional analgesics. Pain is typically the first sensation to go, the last to return. For a more detailed explanation: The primary effect of local anesthetics is intraneuronal blockade of voltage channel-gated Na channels. Progressively increasing concentrations of local anesthetics result in an increased threshold of excitation, a slowing of impulse conduction, a decline in the rate of rise of the action potential, a decrease in the height of the action potential, and eventual obliteration of the action potential. Local anesthetics first block small unmyelinated or lightly myelinated fibers (pain), followed by heavily myelinated but small-diameter fibers, and then larger-diameter fibers (proprioception, pressure, motor). At high serum concentrations autonomic nerve function can be affected. At toxic concentrations other excitable tissues (cardiac, smooth, skeletal muscle) can be affected.

5. The answer is A. First-order neurons that convey pain and temperature sensations to the spinal cord terminate principally in the ipsilateral laminas I and II upon dendrites of cells located in adjacent laminas.

6. **The answer is B.** Although a rare occurrence, halothane and other inhaled volatile liquid anesthetics may cause malignant hyperthermia, the signs and symptoms of which we have described in the question. Apparently, this occurs mainly in genetically susceptible individuals (whether a personal or familial history, as the predisposition seems to be heritable). The prevalence of the reaction is increased by concomitant use of succinylcholine. Indeed, the halothane-succinylcholine interaction is most commonly cited as the main cause of malignant hyperthermia.

ANSWERS MCQs IFOM

1. **The correct answer is B.** This patient is suffering from lower extremity paralysis and altered sensation after a major surgery on his abdominal aorta. The aorta supplies blood to the spinal cord via the artery of Adamkiewicz, a major branch of which then provides circulation to the anterior spinal artery (ASA). Since the patient had to be stabilized for hemorrhage-and his lab values reflect a low hematocrit-his symptoms are most likely due to decreased blood supply to the anterior spinal cord via the ASA. This is called anterior spinal artery syndrome.

Anterior spinal artery syndrome can affect all ascending and descending pathways except for the dorsal columns, which are located in the most posterior aspect of the spinal cord. Because the dorsal columns are used for proprioception and vibration, these functions should remain intact, whereas all others (pain, temperature, motor functions including urinary and fecal continence) should be decreased. On sensory neurological exam, this patient would then experience decreased pain sensation and normal vibration sense.

Decreased pain sensation (spinothalamic tract) and decreased vibration sense (dorsal columns) could be seen together ina patient with both anterior and posterior spinal cord injury, such as occurs in Brown-Séquard syndrome. Patients will have ipsilateral loss of all sensation at the level of the lesion. Below the lesion, they also experience contralateral loss of pain and temperature sensation, whereas all other sensory/motor pathways are disrupted ipsilaterally.

Decreased vibration sense (carried by the dorsal columns) with normal pain sensation (spinothalamic tract) could be seen in a patient with tabes dorsalis. This condition is a manifestation of tertiary syphilis, resulting from demyelination of the dorsal columns and roots.

Normal sensory findings with abnormal motor exam (decreased strength) could be seen in amyotrophic lateral sclerosis or poliomyelitis. These disorders primarily affect motor neurons while sparing the sensory pathways of the spinal cord.

Decreased ability to sense pain (spinothalamic tract) combined with a normal motor exam might be seen in a patient with syringomyelia. This condition occurs in the upper extremities due to the development of a cystic cavity in the spinal cord called a syrinx.

2. The correct answer is B. This unresponsive 26-year-old man with cardiorespiratory depression, pinpoint pupils non-reactive to light, and needle track marks on his forearm presents a clinical picture that is most consistent with opioid intoxication.

Opioids are analgesics with high potential for addiction. Drugs in this category act as an agonist on the mu receptors which stimulate pain relief along with euphoria and decreased anxiety. Patients also experience respiratory depression, miosis, constipation, and cough suppression. The drugs' rapid onset of action and short half-life lead to addictive behaviors to sustain the euphoria. Opioids also act on k and δ receptors which elicit different symptoms and adverse effects. Activation of k receptors causes dysphoria, hallucinations, miosis, analgesia and sedation. Activation of & receptors causes analgesia, diuresis, and dysphoria.

Opioid abuse has become an epidemic in the United States, with severe overdose leading to respiratory depression, coma, and death. Patients who are addicted to opioids will experience withdrawal symptoms when drug use is discontinued. These include autonomic symptoms (eg, nausea, vomiting, diaphoresis, and diarrhea), sleeplessness, tremors, abdominal cramps, bone pain, and cravings. Management for dependence includes substitution with methadone or buprenorphine and gradual tapering, as well as group therapies and cognitive behavioral therapies. Methadone and buprenorphine act on the same receptor as opioids but have a longer half-life and reduced addictive potential.

Naloxone, which is primarily used in an emergency setting, acts as an antagonist on the u receptor and is used in combination with buprenorphine to manage opioid abuse. Activation of k receptors , which is also precipitated by opioid abuse, causes symptoms of dysphoria, hallucinations, miosis, analgesia, and sedation, but not respiratory depression, Inhibition of $GABA_A$ receptors by flumazenil leads to hypoventilation, convulsions, blurred vision, tinnitus, and diaphoresis. Activation of $GABA_A$ receptors, as by barbiturates and benzodiazepines, leads to sedation, muscle relaxation, respiratory depression, hypotension, nausea, blurred vision, and coma. Atropine inhibits muscarinic receptors which leads to mydriasis, dry skin and mouth, and constipation. Blockade of noradrenergic receptors, which is precipitated by use of cocaine, will lead to mydriasis, agitation, and tactile hallucination.

The physiology of the autonomic nervous system
MCQs STEP 1

1. An elderly female suffering from an infection complained that she could not salivate and was unable to display lacrimation on the right side of her face. Following a neurological examination, it was determined that a peripheral component of a cranial nerve was affected by this disorder. Which of the following cell bodies of origin form the origin of the affected cranial nerve?

A. Dorsal motor nucleus of the vagus
B. Nucleus ambiguus
C. Inferior salivatory nucleus
D. Superior salivatory nucleus
E. Edinger-Westphal nucleus of cranial nerve III

2. Pupil size is an important indicator of brainstem function. Which of the following results in pupillary constriction?

A. Atropine, a blocker of muscarinic receptors
B. Decreased parasympathetic activity of inner eye muscle fibers during darkness
C. General increased sympathetic tone during emotional excitement
D. Increased sympathetic activity of inner eye muscle fibers during darkness
E. Phentolamine, a blocker of alpha adrenergic receptors

3. A53-year-old healthy male undergoes an exercise stress test, running on a treadmill until a maximum exertion is obtained. Which of the following statements correctly describes effects of autonomic nerve activity on the cardiovascular system in such a healthy subject?

A. Inhibition of parasympathetic nerves decreases total peripheral resistance
B. Inhibition of parasympathetic nerves increases heart rate
C. Inhibition of parasympathetic nerves increases total peripheral resistance
D. Stimulation of parasympathetic nerves decreases the strength of cardiac ventricular contractions
E. Stimulation of sympathetic nerves decreases the strength of cardiac ventricular contractions

4. A 20-year-old female tennis player has just won a tennis match on a warm summer day. Her blood pressure at this time is 135/70 with a heart rate of 140 beats per minute and a respiratory rate of 25 per minute. She is flushed and sweating profusely. Compared to the resting state, what can be said about the level of activity of sympathetic nerves to her heart and to her cutaneous vasculature?

A. Both are increased
B. Both are decreased
C. Neither is different from at rest

D. Sympathetic activity to the heart is decreased while that to the cutaneous vasculature is increased

E. Sympathetic activity to the heart is increased while that to the cutaneous vasculature is decreased

MCQs IFOM

1. A 5-year-old boy is brought to the clinic by his mother due to excessive vomiting and sweating. His symptoms began soon after his mother found him eating wild mushrooms. The patient is afebrile; blood pressure is 80/45 mm Hg, pulse is 58/min, and respiratory rate is 16/min. On physical examination, the patient is abnormally drowsy, sweating heavily, and salivating

Which of the following additional findings is associated with activation of the most likely receptor targeted by this toxin?

A. Bronchodilation

B. Decreased gastrointestinal motility

C. Lipolysis

D. Mydriasis

E. Urinary retention

F. Vasodilation

ANSWERS MCQs STEP 1

1. The answer is D. The preganglionic parasympathetic neurons associated with lacrimation and which contribute to salivation arise from the superior salivatory nucleus of the lower pons. These preganglionic neurons synapse with postganglionic neurons in the submandibular and pterygopalatine ganglia. Since the disorder affected parts of the facial nerve, other choices are clearly incorrect since they relate to other cranial nerves. The inferior salivatory nucleus governs salivation associated with the parotid gland but has no relationship to lacrimation.

2. The answer is E. Pupil diameter is determined by the balance between sympathetic tone to the radial fibers of the iris and parasympathetic tone to the circular pupillary sphincter muscle. Sympathetic activation will result in pupillary dilation via activation of alpha-adrenergic receptors. Hence, an alpha-adrenergic blocker leads to constriction of the pupil. Parasympathetic activation on the other hand will result in pupil constriction via activation of muscarinic acetylcholine receptors, so that pupil dilation occurs as a result of a muscarinic acetylcholine receptor block (choice A). The same is true for decreased parasympathetic activity during darkness (choice B), or increased sympathetic activity, independent if the initial stimulus is due to emotional excitement or darkness (choices C and D).

3. The answer is B. Since cardiac SA nodal cells receive tonic input from both sympathetic and parasympathetic nerves, heart rate increases whenever sympathetic firing rate increases or parasympathetic firing rate decreases. In humans, the parasympathetic innervation of ventricular muscle is negligible (choice D), and the strength of contraction increases with increasing preload and with increasing sympathetic firing rate (choice E). With few exceptions, blood vessels are not innervated by parasympathetic nerves, and there is little effect of changes in parasympathetic tone on total peripheral resistance (choices Aand C).

4. The answer is E. During exercise in the heat, blood flow must increase to the actively contracting muscles, as well as the cutaneous vessels to shunt heat from the interior of the body to the skin at the surface of the body. Activation of sweat glands allows cooling via evaporation from the surface of the skin. To increase blood flow to the muscles and the skin, it is necessary to increase sympathetic tone to the heart to increase cardiac output. Most sweat glands are activated by sympathetic cholinergic nerves that are activated during sweating. However, the cutaneous vasculature involved in bringing warm blood to the surface of the skin for cooling is constricted by a strong sympathetic tone at rest. During exercise, when body cooling is necessary, sympathetic tone to these cutaneous capillary loops is reduced, causing vasodilation and increased cutaneous blood flow, thus choice E is appropriate.

ANSWERS MCQs IFOM

1. The correct answer is F. This 5 year-old boy presents with diaphoresis, vomiting, somnolence, bradycardia, and hypotension after ingestion of a wild mushroom, which is most suggestive of muscarinic toxicity. Activation of M3 receptors on endothelial cells results in nitric oxide (NO) production and relaxation of smooth muscle cells, which leads to vasodilation. Activation of M3 Gq coupled receptors activates the IP3-DAG pathway which leads to elevated levels of calcium. In vascular smooth muscle, this results in contraction. In contrast, activation of M3 on endothelial cells leads to smooth muscle relaxation and vasodilation. This is because elevated calcium in endothelial cells stimulates the production of nitric oxide (NO) from L-arginine. NO difuses freely into smooth muscle cells, stimulating the conversion GTPto cGMP, which in turn leads to dephosphorylation of myosin light chain by myosin light chain phosphatase. Dephosphorylation leads to relaxation and vasodilation which results in hypotension. Why incorrect answers are wrong:

Lipolysis can occur from beta-3 adrenergic activation, which is a type of sympathetic activation. However, this patient's symptoms are highly suggestive of parasympathetic activation of M1-M3 receptors.

Bronchodilation can occur from stimulation of β2 adrenergic receptors, which is a type of sympathetic receptor. This patient's symptoms are suggestive of parasympathetic activation.

Urinary retention, mydriasis, and decreased gastrointestinal motility are associated with inhibition of the parasympathetic system (ie, muscarinic antagonism)

Essentially, these symptoms are the opposite of muscarinic activation and include an elevated body temperature, tachycardia, flushing, dry mouth, constipation, urinary retention, and cycloplegia.

CLINICAL CASES

1.Reduced secretion from salivary and lacrimal glands could indicate damage to what nerve?

Reduced salivary and lacrimal gland secretions can indicate damage to the facial nerves, which innervate the submandibular, sublingual, and lacrimal glands. The glossopharyngeal nerves innervate the parotid glands.

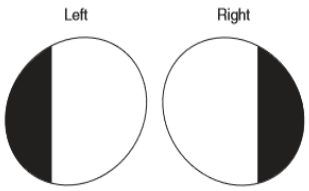
2. A patient has been exposed to the organophosphate pesticide malathion, which inactivates acetylcholinesterase. Which of the following symptoms would you predict: blurring of vision, excess tear formation, frequent or involuntary urination, pallor (pale skin), muscle twitching, or cramps? Would atropine, a muscarinic blocking agent, be an effective drug to treat the symptoms? Explain.

A Inactivation of acetylcholinesterase results in a buildup of acetylcholine in synapses and overstimulation of muscarinic receptors. One would expect mostly parasympathetic effects because the effects of acetylcholine are enhanced: blurring of vision as a result of contraction of ciliary muscles, excess tear formation because of overstimulation of the lacrimal glands, and frequent or involuntary urination because of overstimulation of the urinary bladder. Pallor resulting from vasoconstriction in the skin is a sympathetic effect that would not be expected because skin blood vessels respond to norepinephrine. Muscle twitching or cramps might occur because they normally respond to acetylcholine. Atropine, a muscarinic blocking agent, can be used to treat exposure to malathion.

3. Explain why methacholine, a drug that acts like acetylcholine, is effective for treating tachycardia (heart rate faster than normal). Which of the following side effects would you predict: increased salivation, dilation of the pupils, sweating, or diffi culty in taking a deep breath?

SECTION SPECIAL SENSES
MCQs STEP 1

1. A 59-year-old woman presents with headaches and decreasing vision over the past several months. Her children state that she has been bumping into things recently and does not seem to see them when they are not directly in front of her. Physical examination is unremarkable except for the visual field abnormality illustrated in the picture. Her visual problems are most likely to be caused by a tumor originating in which one of the following anatomic areas?



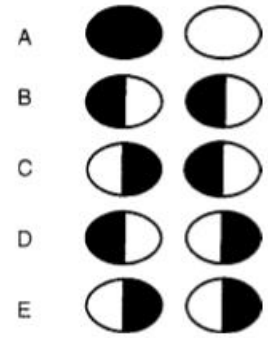
Reproduced from materials USMLE STEP 1

A. Parietal lobe
B. Pineal gland
C. Pituitary gland
D. Posterior orbit
E. Temporal lobe

2. An experiment was performed by a physiologist who was interested in identifying a specific kind of neuron within the visual cortex. The type of neuron sought by the investigator was one that responds to an image in a specific position, has discrete excitatory and inhibitory zones, and is associated with a specific axis of orientation. Which of the following cells would respond to such an image?

A. M cells of the lateral geniculate nucleus
B. P cells of the lateral geniculate nucleus
C. Simple cells of the visual cortex
D. Complex cells of the visual cortex
E. Hypercomplex cells of the visual cortex

3. A 62-year-old woman is referred to a neurologist by her family physician because of a recent loss of initiative, lethargy, memory problems, and a loss of vision. She is diagnosed with primary hypothyroidism and referred to an endocrinologist for treatment of her thyroid problem and to a neuro-ophthalmologist for visual field evaluation. Which of the following visual field defects is most likely to be found?



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4. A patient is admitted to the emergency room after having lost consciousness. Later on, a neurological examination reveals loss of ability to move his right eye laterally when requested to do so. An MRI further reveals the presence of a brainstem infarction. Which of the following is the most likely locus of the infarction?

A. Ventromedial medulla
B. Ventrolateral medulla
C. Dorsolateral pons
D. Dorsomedial pons
E. Dorsomedial midbrain

5. Pupil size is an important indicator of brainstem function. Which of the following results in pupillary constriction?

A. Atropine, a blocker of muscarinic receptors
B. Decreased parasympathetic activity of inner eye muscle fibers during darkness
C. General increased sympathetic tone during emotional excitement
D. Increased sympathetic activity of inner eye muscle fibers during darkness
E. Phentolamine, a blocker of alpha adrenergic receptors

6. A 55-year-old male diabetic has an accommodative power of the lens of 10 dioptres. His near point is located 5 cm (2 in), his far point 10 cm (3.9 in) in front of the eye. Which of the following statements are correct?

A. His corrective lenses are convex
B. His corrective lenses have a positive dioptric value
C. The patient has hyperopia
D. The patient is capable of driving a car without corrective glasses
E. The patient is functionally blind

7. During a routine preschool examination, a 5-year-old boy is found to have difficulty focusing on distant objects. Which of the following is true during far accommodation of the eyes?

A. Ciliary muscles are relaxed
B. Pupils are constricted
C. The focal length of the lens is short
D. The lens is rounded

E. Zonula fibers are relaxed

8. The eye examination of a patient with diabetes mellitus reveals no cataract or glaucoma. The patient's ophthalmoscopic picture of his left eye is shown in the Figure 2-15. Which of the following is most likely affected?

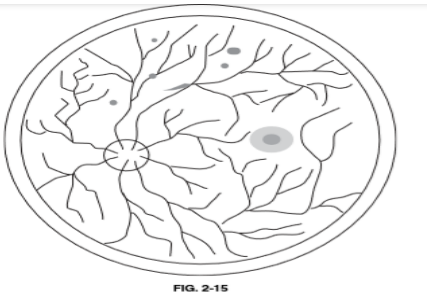

FIG. 2-15

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A. Color vision

B. High acuity vision

C. Near point vision

D. Scotopic vision

E. Spatial vision

9. A 69-year-old man presents with unilateral hearing loss. A lesion in which of the following structures could be responsible for this loss?

A. Inferior colliculus

B. Lateral lemniscus

C. Medial geniculate body

D. Medial lemniscus

E. Organ of Corti

F. Superior olivary nucleus

10. A 24-year-old woman presents after having several "attacks" that last for about 24 h. She states that during these attacks she develops nausea, vomiting, vertigo, and ringing in her ears. Physical examination reveals a sensorineural hearing loss. Which of the following is the most likely cause of this woman's signs and symptoms?

A. Acute suppurative inflammation of the middle ear

B. Dilation of the cochlear duct and saccule

C. Obstruction of the middle ear by a cyst filled with keratin

D. Destruction of the tympanic membrane by a benign neoplasm

E. New bone formation around the stapes and the oval window

MCQs IFOM

1. 63-year-old man comes to his primary care physician for a well- patient examination. During this visit, the patient admits that he is having difficulty hearing his wife clearly when she speaks to him. However, he seems able to hear the cowboys on the television shows he watches, which angers his wife. The physician orders audiology testing but also reassures the patient that his pathology is most likely part of the normal process of aging, and not a newfound aversion to his wife.

Which of the following changes is most likely to be found in this patient?

A. Compression of cranial nerve VIll as it exits the internal auditory meatus

B. Degeneration of the distal hair cells at the apex of the organ of Corti

C. Degeneration of the proximal hair cells of the organ of Corti

D. Degeneration of the utricle and the saccule

E. Trauma to the cochlear nuclei

ANSWERS MCQs STEP1

1. The answer is C. The visual pathway extends from the retina through the optic nerve, then the optic chiasm, through the optic tract, through the lateral geniculate body, and then through the optic radiations of the temporal and parietal lobes to end in the occipital lobes. Lesions in any of these areas produce characteristic visual field defects. For example, bitemporal hemianopsia (loss of vision in the periphery, also called "tunnel vision") is classically produced by lesions that involve the optic chiasm. The pituitary gland, which normally weighs about 0.5 g, lies in a bone depression (the sella turcica) and is covered by dura (diaphragma sellae). Anterior to the diaphragma sellae is the optic chiasm. Pituitary tumors may easily compress the optic chiasm and result in bilateral loss of peripheral vision. Involvement of the optic nerve produces blindness in one eye (mononuclear anopsia), while involvement of the optic tract on one side results in homonymous hemianopsia (loss of the same side of the visual field in both eyes). A lesion involving the temporal lobe optic radiations produces a homonymous superior field defect, while a lesion involving the parietal lobe optic radiations produces a homonymous inferior field defect.

2. The answer is C. Cells in the lateral geniculate nucleus respond very much like ganglion cells in the retina because of the point-to-point projection pathway from the retina to the lateral geniculate. Accordingly, lateral geniculate cells have small concentric receptive fields that are either on-center or off-center in which the cells respond best to small spots of light that are in the center of the receptive field. On the other hand, cells in the visual cortex display a much greater complexity in their responses to images in the visual field. Instead of responding to small spots of light, they respond to lines and borders in the different areas of the visual field. In particular, the simple cell responds as a function of the retinal position in which the line-stimulus is located, as well as its orientation (e.g., whether it is in a vertical or horizontal position). As a result, when a bar of light is positioned in the appropriate part of the visual field with the appropriate orientation, the cells in area 17 will respond maximally. When either of these parameters is altered, the firing pattern of the cell will be reduced or totally inhibited. Complex cells lack clear excitatory and inhibitory zones (i.e., these neurons respond to bars of light in a given orientation but they are not position specific). Hypercomplex cells are stimulated by bars of light of specific lengths or by specific shapes.

3. The answer is D. The optical field defect is produced by an enlarged pituitary gland, which impinges on the optic chiasm. Compression of the optic chiasm by the pituitary gland damages the nasal portion of each optic nerve, which produces a loss of vision in the temporal visual field of both eyes. This defect is referred to as a bitemporal hemianopia.

4. The answer is D. The patient was suffering from a lateral gaze paralysis resulting from an infarction of the dorsomedial pons, thus affecting the abducens nerve (cranial nerve VI), whose nucleus is located in the region of the infarction. The fibers of the abducens nerve pass ventrally, exiting the brain in a relatively medial position at the level of the lower pons.

5. The answer is E. Pupil diameter is determined by the balance between sympathetic tone to the radial fibers of the iris and parasympathetic tone to the circular pupillary sphincter muscle. Sympathetic activation will result in pupillary dilation via activation of alpha-adrenergic receptors. Hence, an alpha-adrenergic blocker leads to constriction of the pupil. Parasympathetic activation on the other hand will result in pupil constriction via activation of muscarinic acetylcholine receptors, so that pupil dilation occurs as a result of a muscarinic acetylcholine receptor block (choice A). The same is true for decreased parasympathetic activity during darkness (choice B), or increased sympathetic activity, independent if the initial stimulus is due to emotional excitement or darkness (choices C and D).

6. The answer is E. Functionally blind means that a person has a visual impairment, that does not qualify as "legally blind" but results in substantial impediment. With a near point of 5 cm and a far point of 10 cm, the man has a severe case of myopia, not hyperopia as stated in choice C. The total convergence power of the relaxed eye with normal vision is approximately 60 dioptres, and the cornea accounts for more than two-thirds of that (40 dioptres). The accommodative power of the lens is about 20 dioptres in the very young, about 10 dioptres at age 25, and would be around 1 dioptre at the patient's age, if he had normal vision. For young adults with normal vision, the near point is about 10 cm from the eye; the far point is at infinity. The corrective lenses for the myopic eye are concave, not convex (choice A). Concave lenses compensate for the excessive positive dioptres of the myopic eye. These lenses are thin in the middle and wide at the edges and have negative dioptric values, not positive ones (choice B). The patient definitely won't be able to drive a car or perform other activities that require fast accommodation without corrective glasses (choice D).

7. The answer is A. This patient probably suffers from myopia (nearsightedness). Myopia is either due to eyeballs that are too long or a lens that is too strong. To focus a distant object onto the retina (far accommodation), the lens has to decrease its refractive power (i.e., increase its focal length). This is accomplished through relaxation of the ciliary muscles that oppose the pull of the sclera, resulting in a tightening of the zonula fibers and a flattening of the lens. Shortening of the focal length (choice C), rounding of the lens (choice D), and relaxation of the zonular fibers (choice E), all occur during near accommodation. The pupils also constrict during near accommodation (choice B), perhaps to increase depth of field

8. The answer is D. The picture, representing the back of the retina as seen through the ophthalmoscope, shows a normal optic disk, a normal macula lutea, and no obvious neovascularization. On the other hand, there are dot hemorrhages as well as one flame-shape hemorrhage site present in the peripheral retina. This indicates an early stage of diabetic retinopathy, known as background retinopathy, in which microaneurysms occur due to damage of existing blood vessels. Since the damage occurred in the peripheral retina, rod vision, also called scotopic vision, is affected. There is no obvious damage yet in the macula lutea and the fovea centralis. At these places, cones are found in the greatest number. Since cones are responsible for color vision, choice Ais incorrect. Since the fovea centralis is the place for high acuity vision, choice B is incorrect. Changes in near point vision (choice C) indicate an error in the refractive power of the eye which is associated with abnormalities at the cornea, the lens, or the geometry of the eyeball. Spatial vision (choice E) refers to the ability to discriminate between spatially defined features. It is mainly determined by visual neuronal networks that enhance visual acuity and contrast, which are both associated with photopic vision.

9. The correct answer is E. The sequence of the auditory pathway is as follows: Organ of Corti → spiral ganglion in the cochlea → vestibulocochlear nerve (CN VIII) → cochlear nuclei (dorsal and ventral) → superior olivary nuclei → lateral lemniscus → inferior colliculus → medial geniculate nucleus of the thalamus (MGN) → primary auditory cortex (Heschl's gyrus). Each ear projects to both sides of the brainstem and cortex via multiple commissures, including the trapezoid body (which contains fibers crossing contralateral to the superior olivary nucleus), the commissure of the inferior colliculus (connecting the right and left inferior colliculi), and another commissure that connects the right and left nuclei of the lateral lemniscus. Therefore, a lesion of any structure up until the superior olivary nuclei will produce an ipsilateral deafness. The only structure listed that is proximal to the superior olivary nuclei is the organ of Corti (choice E). The inferior colliculus (choice A), the lateral lemniscus (choice B), the medial geniculate body (choice C), and the superior olivary nucleus (choice F) all receive information from both ears, and unilateral hearing loss could not result from a lesion of any of these structures. The medial lemniscus (choice D) is not a part of the auditory system. It is part of the somatosensory system, which conveys proprioception, discriminative touch, and vibration information. More specifically, neurons of the gracile and cuneate nuclei send projections that decussate as the internal arcuate fibers and ascend as the medial lemniscus to synapse in the ventroposterolateral nucleus (VPL) of the thalamus.

10. The answer is B. Ménière's disease is an abnormality that is characterized by periodic episodes of vertigo that are often accompanied by nausea and vomiting, sensorineural hearing loss, and tinnitus (ringing in the ears). These symptoms are related to hydropic dilation of the endolymphatic system of the cochlea. Inflammation

of the middle ear (otitis media), which occurs most often in children, may be acute or chronic. If otitis media is caused by viruses, there may be a serous exudate, but if it is produced by bacteria, there may be a suppurative exudate. Acute suppurative otitis media is characterized by acute suppurative inflammation (neutrophils), while chronic otitis media involves chronic inflammation with granulation tissue. Chronic otitis media may cause perforation of the eardrum or may lead to the formation of a cyst within the middle ear that is filled with keratin, called a cholesteatoma. The name is somewhat of a misnomer, as cholesterol deposits are not present. Otosclerosis, a common hereditary cause of bilateral conduction hearing loss, is associated with formation of new spongy bone around the stapes and the oval window . Patients present with progressive deafness. Tumors of the middle ear are quite rare, but a neoplasm that arises from the paraganglia of the middle ear (the glomus jugulare or glomus tympanicum) is called a chemodectoma. Other names for this tumor include nonchromaffin paraganglioma and glomus jugulare tumor. This lesion is characterized histologically by lobules of cells in a highly vascular stroma (zellballen). A similar tumor that occurs in the neck is called a carotid body tumor.

ANSWERS MCQs IFOM

1. The answer is C. The auditory system mediates the sense of hearing, or the process of converting mechanical sound waves to a neuronal stimulus that is registered by the brain. A specialized structure, the organ of Corti, carries out this complex function in a stepwise manner. Sound waves enter into the external auditory canal and vibrate the tympanic membrane, which transfers those waves to the ossicles of the middle ear (malleus, incus, stapes). The ossicles amplify and transmit the sound waves into the perilymph of the scala vestibule via the oval window, with the waves vibrating through the perilymph, causing displacement of the basilar membrane. Displacement of the basilar membrane results in bending of stereocilia (the mechanosensing organelles of hair cels), whose tips are attached to the tectorial membrane. Mechanically gated potasium (K) channels on the tips of stereocilia open when stretched, causing K influx and depolarization, triggering voltage gated calcium (Ca2) channels to open. This Ca2 influx into the hair cell causes release of excitatory neurotransmitters from synaptic vesicles, which diffuse through the perilymph to spiral ganglia neurites.

Age-related degeneration of the organ of Corti (or presbycusis) is a type of sensorineural hearing loss that is part of the normal aging process. It is the most common cause of sensorineural hearing loss in the elderly and manifests with gradually worsening high-frequency hearing loss. The cause of presbycusis is degeneration of the proximal hair cells of the organ of Corti (depicted in the drawing), which lie in the proximal portion of the basilar membrane (farthest from the helicotrema or apex and

closest to the ossicles and oval window). This is the thinnest and least compliant portion of the basilar membrane and is responsible for sensing high-frequency sounds.

The patient in the vignette has a classic presentation of presbycusis: progressively more trouble hearing high-pitched sounds (like his wife's voice) while clearly hearing the voices of most other characters (such as cowboys with low-pitched voices). Tinnitus and dizziness may also be present in some patients. Hearing loss is evaluated with physical exam and audiogram. Management includes reassurance, hearing aids, or cochlear implantation.

Distal hair cell degeneration would lead to low-pitch hearing loss, the opposite of what is occurring in this patient.

Degeneration of the utricle and saccule lead to vertigo, which is absent in the patient.

CN VIII compression would lead to unilateral deafness and symptoms of vertigo.

Unilateral deafness would occur in cochlear nuclei trauma.

CLINICAL CASES

1. A 16-year-old high school student goes to see the school nurse because of severe eye pain and a feeling that there is something "stuck" in his right eye. He does not wear contact lenses. He reports that he was recently working with machines in shop class without wearing protective goggles. Ophthalmologic examination reveals no visible foreign body in the eye; visual acuity is slightly decreased at 20/30; pupils are equal, round, and reactive to light bilaterally; corneal reflex is intact; and extraocular muscles are intact, although the student says his right eye hurts when he moves it.

1.1 What is the most likely diagnosis?

The student has a corneal abrasion, which typically presents with significant eye pain and a foreign body sensation. the patient will also have photophobia. this patient's history suggests the source for his eye injury: working with machinery without wearing protective eyewear. Other etiologies of acute unilateral vision impairment are optic neuritis, retinal detachment or tear, giant cell arteritis, and amaurosis fugax.

1.2 What is the pathway of the corneal blink reflex?

The excruciating pain experienced by this patient is due to the rich innervation of the cornea by the ophthalmic branch of cranial nerve (CN) V (V1). this nerve constitutes the afferent portion of the corneal blink reflex. after synapsing in the sensory nucleus of CN V, there is bilateral projection to the nucleus of CN VII. From there, motor neurons project to the orbicularis oculi muscles, causing a consensual blink response.

1.3 What space lies between the cornea and the lens?

The space between the cornea and the lens is the anterior compartment, which is subdivided by the iris into the anterior chamber and the posterior chamber (Figure 10-4). the entire anterior compartment is filled with aqueous humor, which is secreted by the ciliary body.

1.4 What space lies behind the lens?

Behind the lens is the posterior compartment (Figure 10-4), which is filled with vitreous humor, a gelatinous substance. at the anterior aspect of the posterior compartment, the lens is held in place by the suspensory ligament, which extends from the ciliary body of the choroid to the lens.

1.5 From what embryologic structures do the cornea, iris, ciliary body, lens, and retina develop?

The optic cup is an embryologic structure derived from neuroectoderm that gives rise to the retina, iris, and ciliary body. the lens is derived from surface ectoderm. the inner layers of the cornea are derived from mesenchyme, and the outer layer derives from the surface ectoderm.

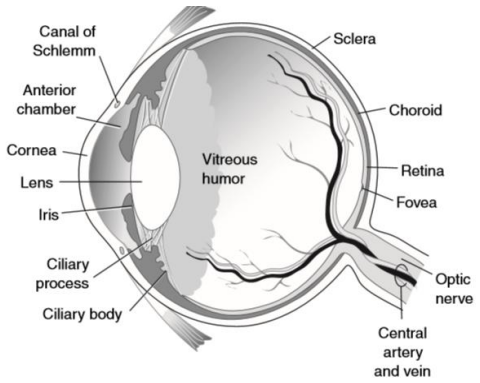

FIGURE 10-4. **The eye and retina.** (Reproduced, with permission, from Le T, Bhushan V, Tolles J. *First Aid for the USMLE Step 1: 2011*. New York: McGraw-Hill, 2011: 420.)

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2. A 70-year-old man with a history of hypertension goes to his ophthalmologist for a routine eye examination. He has needed to wear eyeglasses while driving since he was 18 years of age. Ocular examination reveals increased intraocular pressure in both eyes. On a field test, there is significant loss of peripheral vision, and funduscopic examination reveals cupping.

2.1 What is the most likely diagnosis?

Open-angle glaucoma is the most common form of glaucoma in the United States (90%) and presents as progressive, painless visual loss. Closed-angle glaucoma is painful and can cause additional symptoms such as seeing halos around lights and red eye.

2.2 What is the pathophysiology of this condition?

Open-angle glaucoma is caused by elevated intraocular pressure resulting from obstruction of flow of aqueous humor through the normal outflow channels (Figure 10-9).

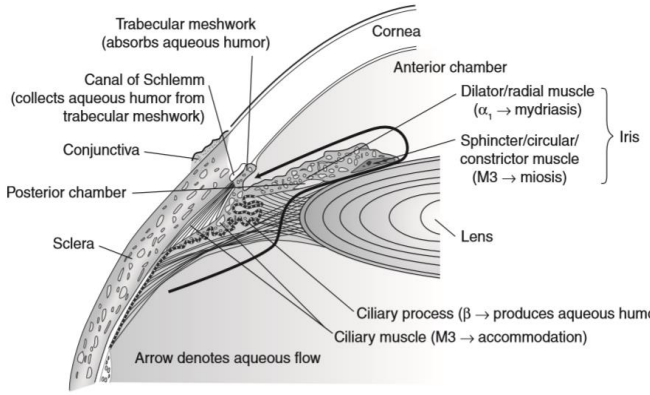

FIGURE 10-9. **Aqueous humor pathways.** (Reproduced, with permission, from Le T, Bhushan V, Tolles J. *First Aid for the USMLE Step 1: 2011*. New York: McGraw-Hill, 2011: 420.)

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2.3 What are the appropriate treatments for this condition?

The direct cholinergic agonists pilocarpine and carbachol are used to treat open-angle glaucoma. these agents act by stimulating ciliary muscle contraction, thereby relieving

tension in the suspensory ligament. Cholinomimetics also stimulate the sphincter pupillae of the iris, which widens the canal of Schlemm and constricts the pupil (miosis). adverse effects include nausea, vomiting, diarrhea, salivation, sweating, vasodilation, and bronchoconstriction.

2.4 What effect does pilocarpine have on cardiac muscle?

Pilocarpine is an M3/M2 muscarinic receptor agonist. Cardiac cells have M2 receptors that, when activated, stimulate a G protein that inhibits adenyl cyclase and increases potassium conductance. pilocarpine stimulation decreases the heart rate and the force of contraction (negative inotrope).

2.5 What additional classes of drugs are useful in treating this condition?

Other drug classes used to treat open-angle glaucoma include the following: • adrenergic agonists such as epinephrine. • β-Blockers and acetazolamide (a carbonic anhydrase inhibitor), which decrease aqueous humor secretion. • prostaglandins, which increase the outflow of aqueous humor.

3. A 10-year-old boy is brought to his pediatrician because of a painful ear. The pain began 1 week earlier with a runny nose and sinus pressure that progressed to ear pain and dizziness. Otoscopic examination reveals the findings in Figure 10-24. He has a low-grade fever of 37.8°C (100.0°F) but no other physical findings.

3.1 What is the most likely diagnosis?

Acute otitis media. the bulging, red tympanic membrane is a sign of middle ear infection. the clinical course suggests a viral upper respiratory infection leading to secondary involvement of the middle ear due to inflammation and congestion of the eustachian tube. the eustachian tube connects the middle ear to the nasopharynx.

3.2 From what embryologic structure is the tympanic membrane derived?

The tympanic membrane derives from the first pharyngeal membrane. the pharyngeal membranes constitute the tissue between the pharyngeal groove, or cleft, and the pharyngeal pouch. Only the first pharyngeal membrane is retained in the adult; the rest are obliterated during development.

3.3 What three bones are located in the middle ear?

The three bones located in the middle ear (auditory ossicles) are the malleus, incus, and stapes); together, they transmit sound from the tympanic membrane to the internal ear. the malleus, which articulates with the tympanic membrane, derives from the first branchial arch. the incus, which lies between the malleus and the stapes, derives from the first branchial arch. the stapes, which articulates with the oval window of the inner ear, derives from the second branchial arch.

3.4 What two muscles control the movement of the bones of the middle ear?

The tensor tympani inserts on the malleus and dampens the amplitude of the tympanic membrane oscillations, which prevents damage to the inner ear from loud sounds. Innervation is by the mandibular nerve (CN V3). the stapedius inserts onto the neck of

the stapes and dampens movement of this ossicle. It is innervated by the facial nerve (CN VII). a lesion denervating the stapedius causes hypersensitivity to sound.

3.5 What organisms commonly cause pediatric ear infections?

In order of prevalence, common bacteria that cause middle ear infection are Streptococcus pneumoniae, Haemophilus influenzae (although rarely type B since the introduction of the conjugated vaccine), and Moraxella catarrhalis. appropriate antibiotic coverage involves a β-lactamase such as amoxicillin. Less common organisms are group a streptococci, Staphylococcus aureus, Pseudomonas, and in newborns, gram-negative bacilli. approximately 15%–20% of middle ear infections are due to viruses, including respiratory syncytial virus, rhinovirus, influenza viruses, and adenovirus.

SECTION ENDOCRINE SYSTEM
MCQs STEP 1

1. A 61-year-old woman develops purple striae on her abdomen and a rounded facial appearance. She has smoked two packs of cigarettes a day for the past 40 years. Chest x-ray shows a 4-cm, centrally located lung mass. This mass is most likely producing a hormone that promotes the production of cortisol by stimulating which of the following reactions?

A. 11-Deoxycortisol to cortisol
B. 17-Hydroxyprogesterone to 11-deoxycortisol
C. Cholesterol to pregnenolone
D. Pregnenolone to progesterone
E. Progesterone to 17-hydroxyprogesterone

2. A 45-year-old man has a blood pressure reading of 160/100 mm Hg on three separate visits. He refuses to take antihypertensive medication but is willing to modify his lifestyle in an effort to lower his blood pressure. He quits smoking, joins a health club, and greatly reduces salt from his diet. Which of the following areas of the adrenal gland would be expected to increase in activity because of his diet?

A. Adrenal medulla
B. Zona fasciculata of the adrenal cortex
C. Zona glomerulosa of the adrenal cortex
D. Zona reticularis of the adrenal cortex

3. A 49-year-old woman comes to the clinic complaining of fatigue. She denies fever, vomiting, or diarrhea, but physical examination shows dry mucous membranes. Her blood pressure is 90/60 mm Hg. Laboratory studies show a plasma sodium level of 129 mEq/L and a potassium level of 5.5 mEq/L. Which of the following is the most likely cause of her hyponatremia?

A. Addison disease
B. Diabetes insipidus
C. Hyperaldosteronism
D. Psychogenic polydipsia
E. Syndrome of inappropriate ADH secretion

4. A 47-year-old man presents with headaches, muscle weakness, and leg cramps. He is not currently taking any medications. Physical examination finds a thin adult man with mild hypertension. Laboratory examination reveals slightly increased sodium, decreased serum potassium level, and decreased hydrogen ion concentration. Serum glucose levels are within normal limits. A CT scan reveals a large tumor involving the cortex of his left adrenal gland. Which of the following combinations of serum laboratory findings is most likely to be present in this individual?

A. Decreased aldosterone with increased renin
B. Decreased cortisol with decreased acth
C. Increased aldosterone with decreased renin
D. Increased cortisol with increased acth
E. Increased deoxycorticosterone with increased cortisol

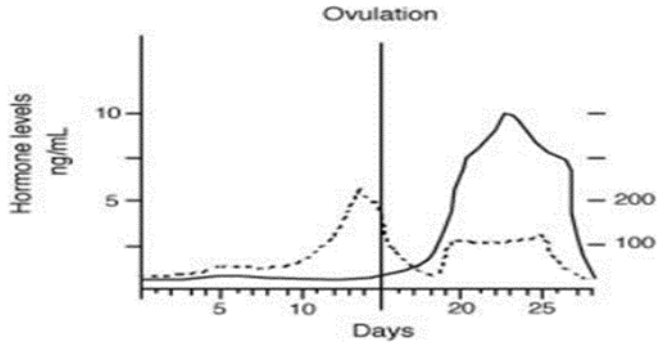
5. The hands and nails of a 45-year-old woman show the discolorations. The woman states that she had pulmonary tuberculosis about 10 years ago. The clinician prescribes cortisol, but counsels her that as a side effect it might lead to thin skin and thinning of her limbs because of an increase in which of the following?
A. Adrenocorticotropic hormone (acth) secretion
B. Corticotrophin-releasing hormone (crh) secretion
C. Insulin sensitivity in muscle
D. Protein degradation
E. Wound healing

6. A 4-year-old child with signs of precocious (early onset) puberty is brought to a clinic for evaluation and found to have a congenital deficiency of 21-β-hydroxylase. Feedback inhibition of the pituitary gland is lost and excess ACTH is secreted. As a result, which of the following happens?
A. Adrenal cortical atrophy occurs
B. Adrenal medullary hypertrophy occurs
C. Excess cortisol is released
D. Precursors to cortisol synthesis increase
E. Serum cholesterol falls dramatically

7. A 55-year-old woman stopped menstruating approximately 3 months ago. Worried that she may be pregnant, she decides to have a pregnancy test. The result is negative. Which of the following series of test results will confirm that the woman is postmenopausal?
A. Decreased LH, decreased FSH, increased estrogen
B. Decreased LH, increased FSH, decreased estrogen
C. Increased LH, decreased FSH, decreased estrogen
D. Increased LH, increased FSH, decreased estrogen
E. Increased LH, increased FSH, increased estrogen

8. To make extra money, a medical student participates in a study to determine hormone levels during the menstrual cycle. Her menarche was at age 13, and she has always had regular, 28-day cycles. When analyzing the results of her studies, it is

correct to assume that the dotted line in the figure secretion pattern of



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A. Estrogen

B. Follicle-stimulating hormone (FSH)

C. Gonadotropin-releasing hormone (GnRH)

D. Luteinizing hormone (LH)

E. Progesterone below represents the cyclic

9. A newlywed 23-year-old woman and her 28year-old husband are evaluated for infertility. They have been unable to conceive a child despite regular intercourse for the past 12 months. The first step of this couple's infertility workup is to determine whether ovulation occurs regularly. Which of the following hormones is directly responsible for ovulation?

A. Estradiol

B. Estriol

C. Follicle-stimulating hormone (FSH)

D. Inhibin

E. Luteinizing hormone (LH)

10. Figure 2-26 shows the conversions of cholesterol into the hormones C and D within follicular cells of the ovary (large arrows) and the regulation of these processes (small arrows) by pituitary hormones (A, B, E), when binding to their receptors on the cell surfaces (dark squares). Which of the letters in the figure best represents the hormone the concentration of which in serum changes in the following way?

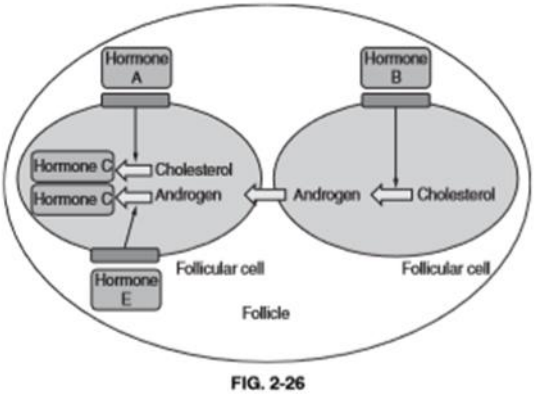

FIG. 2-26

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Concentration during follicular phase of the menstrual cycle: 70 pg/mL Concentration during preovulatory period of the menstrual cycle: 320 pg/mL Concentration during luteal phase of the menstrual cycle: 130 pg/mL Postmenopausal concentration: 10 pg/mL

A. A

B. B

C. C

D. D

E. E

11. A 69-year-old alcoholic has had severe, progressively increasing epigastric pain for the past 24 hours. He has been nauseous, and he vomited three times. Laboratory studies show hypocalcemia and metabolic hypochloremic alkalosis. The primary metabolic effect of the principal hormone secreted by the alpha cells of this organ is

A. Augmentation of calcium deposition in bone

B. Increase of amino acid storage in the liver

C. Promotion of lipogenesis in liver and adipose tissue

D. Inhibition of gluconeogenesis

E. Stimulation of glycogenolysis

12. A patient presents with Whipple's triad, including plasma glucose <60 mg/dL, symptomatic hypoglycemia, and improvement of symptoms with administration of glucose. CT of the abdomen shows enlargement of the islet cells suggestive of islet cell carcinoma. Which of the following is true regarding the islets of Langerhans?

A. They are found primarily in the head of the pancreas.

B. They constitute approximately 30% of the pancreatic weight.

C. They contain six distinct endocrine cell types.

D. They have a meager blood supply.

E. They secrete insulin and glucagon.

13. A series of photographs taken of a middle-aged man over a period of 2 decades demonstrates gradual coarsening of facial features and progressive protrusion of the brows. Upon questioning, the patient reports having to wear larger shoes than he did as a young man. Which of the following pair of hormones normally regulates the hormone responsible for these changes?

A. Dopamine and norepinephrine

B. LH and hCG

C. Prolactin and FSH

D. Somatostatin and GHRH

E. TSH and ACTH

14. A 65-year-old woman receives 3 liters of 0.9% saline following a minor surgical procedure. This results in increased right atrial filling and contraction. Which of the following is most likely to be secreted in response?
A. Aldosterone
B. Antidiuretic hormone (ADH)
C. Atrial natriuretic factor (ANF)
D. Norepinephrine
E. Renin
15. A 34-year-old male is brought into the emergency room, having been found unconscious in his apartment. Apparently, he has been in this state for 2 days. The laboratory values for the patient's blood and urine are consistent with elevated circulating antidiuretic hormone (ADH). Which one of the following will directly stimulate ADH in this patient?
A. Angiotensinogen
B. Extracellular fluid osmolality increase
C. Temperature decrease
D. Thyroid hormone
E. Volume increase
16. A very thin 15-year-old female presents with headache, polyuria, and grand mal seizures. She answers the question, if she has had to vomit recently, with "frequently" but that these symptoms "are under control now." Her body mass index is 14.1. Serum glucose, calcium, and potassium are normal. Serum sodium, chloride, and osmolarity are low. As a working diagnosis, which of the following is most likely?
A. Addison disease
B. central diabetes insipidus
C. diabetes mellitus
D. nephrogenic diabetes insipidus
E. water intoxication
17. High-dose glucocorticoid therapy for treatment of rheumatoid arthritis remains highly controversial. It is widely agreed that it is highly effective in controlling acute rheumatoid inflammation, but it may also result in significant adverse effects. Complications of high-dose glucocorticoid therapy include which of the following?
A. Excessive growth in children and acromegaly in adults
B. Hyperkalemia
C. Hyponatremia
D. Suppression of the hypothalamicpituitary-adrenal axis
E. Volume depletion
18. A 23-year-old Caucasian male is admitted to the hospital following a motorcycle accident. On examination, no bones appear to be broken, but there is extensive muscle

bruising resulting in tissue swelling from increased capillary permeability. His arterial blood pressure is 80/40. He is awake and able to walk with assistance. Based on this information, it is likely that which of the following will be decreased from normal?
A. Circulating levels of catecholamines
B. Left atrial pressure
C. Plasma aldosterone concentration
D. Plasma lactate concentration
E. Plasma renin activity
19. A motor vehicle accident caused complete pituitary stalk transection. Secretion of all pituitary hormones is lost except for one, the blood level of which actually increases. Which one of the following pituitary hormones is distinctive in that its primary control is by inhibition rather than stimulation by the hypothalamus?
A. Gonadotropin-releasing hormone
B. Growth hormone
C. Prolactin
D. Proopiomelanocortin
E. Thyroid-stimulating hormone
20. A 55-year-old male presents with headache and visual field changes. He is six-and-a-half feet tall and has a puffy face. His skin on hands and feet is thickened, and compared to a picture of him at age 30, his nose, ears, and jaw seem larger. His teeth are separated (diastema). He seems to sweat more and complains of bad sleep. Which of the following would provide the greatest therapeutic benefit to this patient?
A. GHRH
B. Growth hormone
C. Insulin
D. Somatostatin
E. Thyroid hormones
21. A person has an elevated plasma osmolality and reduced plasma ADH level and excretes a large volume of osmotically dilute urine. The urine contains no glucose. What is the most likely explanation for this situation?
A. Congestive heart failure
B. Nephrogenic diabetes insipidus
C. Neurogenic diabetes insipidus
D. Primary polydipsia
E. Uncontrolled diabetes mellitus

MCQs IFOM

1. A researcher who studies endocrine tumors is attempting to develop new methods to treat hypertensive crisis in patients with pheochromocytoma. She plans to run an experiment using rats to simulate conditions of crises that arise during surgery. She plans to anesthetize the rats and then administer a high-potency injection that will lead to hyperstimulation of the adrenal gland.

If properly targeted, which of the following molecules would most likely be used in this injection?

A. Acetylcholine
B. Cortisol
C. Dopamine
D. Epinephrine
E. Norepinephrine

2. An 18-yearold woman is referred to a specialist because she has not yet begun to menstruate. She reports generalized weakness and occasional bouts of nausea and vomiting. Her blood pressure is 160/99 mm Hg, heart rate is 92/min, and respiratory rate is 16/min. Physical examination is noticeable for the lack of breast development consistent with Tanner stage 1. Laboratory studies show a serum potassium level of 2.2 mEq/L. She is diagnosed with a condition that decreases the production of two of the three major adrenal steroid hormones, leading to an excess of on ly one functioning hormone. In which area of the adrenal gland is this one functioning steroid hormone produced?

A. Capsule
B. Medulla
C. Zona fasciculata
D. Zona glomerulosa
E. Zona reticularis

3. A healthy 21-year-old woman with no history of significant illness comes to the physician requesting combination oral contraceptives. She is sexually active and always uses condoms as contraception. She has no history of migraines and no personal or family history of clotting disorders. Blood pressure is 123/76 mm Hg, height is 172 cm (5 ft 7 in), weight is 68 kg (150 Ib), and body mass index is 23 kg/m2. No abnormalities are noted on physical examination. The result of a urine test for B-human chorionic gonadotropin is negative. The physician decides to prescribe combination oral contraceptives for the patient, which will decrease the amount of endogenous follicle-stimulating hormone (FSH) produced. Which of the following will most likely be affected immediately?

A. Blastocyst implantation
B. Change in estrogen concentration during follicular phase

C. Fertilization of ovum
D. Midcycle surge of luteinizing hormone
E. Ovulation
4. A young couple presents to a fertility clinic, reporting that they have been attempting to conceive a child for the last 16 months without success. The 25-year-old wife's infertility work-up reveals regular menstrual cycles, viable oocytes, and no hormonal irregularities. However, the 27-year-old husband's semen analysis is consistent with low sperm count, and physical examination reveals tall height (76 in/193 cm), sparse body hair, small and firm testes, and mild gynecomastia. A karyotype analysis on the husband is performed and results are pending.
Which of the following laboratory results is most consistent with this man's condition?
A. Decreased follicle-stimulating hormone level
B. Decreased gonadotropin-releasing hormone level
C. Increased luteinizing hormone level
D. Normal follicle-stimulating hormone level
5. A 33-year-old man comes to the fertility clinic accompanied by his 29-year-old wife. The couple have been struggling to conceive for the past 1.5 years despite ovulation tracking and frequent intercourse. The patient's medical history is significant for attention-deficit hyperactivity disorder, and his surgical history includes an operation for an undescended testicle at age 2 years. His current medications include occasional ibuprofen and a multivitamin. On examination, the patient's vital signs are normal. He is tall with long extremitiesand has minimal facial and body hair. Breasts are enlarged, and testes are small and firm. Laboratory work shows elevated luteinizing hormone (LH) and follicle-stimulating hormone (FSH) levels.
Which of the following is most directly responsible for this patient's high levels of FSH?
A. Abnormal Leydig cell function
B. Decreased levels of inhibin B
C. Inactive cells in the interstitium of the testicles
D. Low levels of testosterone
E. Presence of an inactivated X chromosome
6. A 52-yearold woman presents to her physician reporting "occasional" feelings of warmth with sweating and a rapid heartbeat. She takes no medications and has a history of hypertension controlled by exercise and diet. Reproductive history includes two pregnancies resulting in live births. Her last menstrual period was 1 year ago, which is about when her symptoms began. Her vital signs are all within the normal range. Speculum examination reveals decreased vaginal rugae and some dryness. The remainder of the findings of the bimanual and physical examinations are unremarkable. Urine B-human chorionic gonadotropin is found to be negative. Her physician

considers initiating hormone replacement therapy (HRT). In addition to relief of her current symptoms, which of the following would most likely be observed with estrogen-progestin combined HRT?

A. Decreased incidence of stroke and myocardial infarction

B. Decreased risk of cervical cancer

C. Decreased risk of invasive breast cancer

D. Decreased risk of osteoporotic fracture

E. Increased risk of uterine cancer

7. A 18-year-old woman presents to her physician because she has not had a menstrual period for the past 6 months. She states that she first had her period at 12 years of age and that she began having it at regular 30-day intervals when she was 14 years of age. On initial examination, the woman is 57 and approximately 200 Ib (90 7kg, BMI: 31)

Laboratory tests show:

Testosterone: 150 ng/dL

Estradiol: 650 pg/mL

Follicle-stimulating hormone: 6 miU/ml

Luteinizing hormone: 30 mlU/mL

Hormone reference ranges for females	
Total testosterone	0-5 months: 20-80 ng/dL 6 months-9 years: <7-20 ng/dL 10-11 years: <7-44 ng/dL 12-16 years: <7-75 ng/dL 17-18 years: 20-5 ng/dL
Estradiol	Mid-follicular phase 27-123 pg/mL Periovulatory: 96-436 pg/mL Mid-luteal phase: 49-294 pg/mL Follicle-stimulating hormone Premenopause: 4-20 mlU/mL 6 months-9 years: <7-20 ng/dL 10-11 years: <7-44 ng/dL 12-16 years: <7-75 ng/dL 17-18 years: 20-5 ng/dL
Estradiol	Mid-follicular phase 27-123 pg/ml Periovulatory: 96-436 pg/mL Mid-luteal phase: 49-294 pg/mL

	Follicle-stimulating hormone Premenopause: 4-20 mlU/mL Midccyle peak: 10-90 mlU/mL Postmenpause: 40-250 mlU/mL
Luteinizing hormone	Follicular phase: 5-30 mlU/mL Midcycle: 75-150 mlU/mL Postmenopause: 30-300 mlU/mL

Which of the following additional laboratory values will most likely be altered in this patient?

A. Cancer antigen 125

B. Glucose

C. Prolactin

D.Thyroid-stimulating hormone, triiodothyronine, and thyroxine

E. β-human chronic gonadotropin

8. A 25-year old woman who is 39 weeks pregnant presents with a blood pressure of 162/90 mm Hg and a finding of 3+ protein on urine dipstick. She says she has a headache and blurry vision She is not known to be allergic to any medications. The obstetrician immediately admits the patient to the labor and delivery suite and decides to induce labor. The doctor writes a prescription for a medication commonly used for seizure prophylaxis in pregnant patients. Two hours later, the doctor is called to the patient's room, where recent laboratory testing reveals abnormally high levels of this drug. Which of the following additional signs is the patient most likely to exhibit now that the drug level is too high?

A. Hyperactivity

B. Hypertension

C. Hyporeflexia

D. Involuntary movements

E. Nystagmus

F. Rash

9. A 22-year-old woman comes to her primary care physician for her yearly health maintenance examination. She has no notable past medical history, takes no medications, denies smoking or illicit drug use, and has regular 28-day menstrual cycles. She is on day 19 of her current cycle, as measured from the first day of her last menstrual period. Using the table, which of the following represents the current levels (on day 19) of progesterone, estrogen, follicle-stimulating hormone (FSH), and luteinizing hormone (LH) relative to day 1 of this woman's cycle?

Choice	Progesterone	Estrogen	Feedback on LH and FSH
A	Decrease	Decrease	Negative
B	No change	Increase	Negative
C	No change	Increase	positive
D	Increase	Decrease	Negative
E	Increase	Increase	negative

10. A 16-year-old presents to her family physician because she believes she is pregnant. An office pregnancy test confirms her suspicion. The biological marker detected by the blood test to assess pregnancy is most structurally similar to which of the following?
A. The hormone that promotes rupture of the ovarian follicle during ovulation
B. The hormone that promotes the release of cortisol from the adrenal cortex
C. The hormone that promotes the release of thyroid-stimulating hormone from the anterior pituitary
D. The hormone that stimulates milk production from mammary glands
E. The hormone that stimulates uterine contractions during labor
11. A 28-year-old woman, G2P1, comes to the clinic for ultrasonography during her 15th week of pregnancy. She has no history of significant illness and has had an uncomplicated pregnancy She is very interested in leaming the sex of her fetus. The physician informs her that she is having a boy and explains the ultrasound findings.
Which of the following hormones produced the findings that indicated the sex of the baby?
A. Androstenedione
B. Dihydrotestosterone
C. Follicle-stimulating hormone
D. Müllerian inhibiting factor
E. Progesterone
F. Testosterone
12. A53-year-old female presents to her gynecologist with complaint of iregular menstrual periods. She claims that her last menstrual period was 12 months ago, and prior to that she often went 2-3 months without a period. On further questioning, she also admits irritability and intermittent intolerance to heat. Blood tests reveal the hormone serum levels listed in the table.

	Value	Reference range
Estrogen	22 pg/ml	60-400 pg/ml
Follicle-stimulating hormone	100 mIU/L	1-26 mIU/L
Luteinizing hormone	50 mIU/mL	1-12 mIU/mL

Which of the following is most likely the primary cause of this patient's symptoms?
A. Decreased estrogen levels
B. Decreased thyroid-stimulating hormone levels
C. Increased follicle-stimulating hormone levels
D. Increased progesterone levels
E. Increased testosterone levels
13. A 48-year-old woman presents to her primary care provider for her annual well-woman physical examination. She reports experiencing 2- to 3-minute episodes of feeling "really hot across her chest and face, a sensation that spreads to her entire body. She has noticed increased frequency of these episodes at night because they sometimes awaken her. On further questioning, she admits to increased discomfort and dryness with intercourse. Review of systems is negative for fever, unexplained weight loss, or respiratory symptoms. Results of physical and pelvic examinations demonstrate mildly atrophic mucosa of the vagina with no other significant abnormalities. A complete blood count is performed, and the relarilts include:
Hemoglobin: 15.4 g/dL
Hematocrit 46.0%
WBC count 5900/mm
Platelets 301,000/mms
Which of the following sets of hormone changes is most likely to be seen in this patient compared with testing performed 10 years ago?

	LH	FSH	Estrogen
A	Decrease	Decrease	Decrease
B	Decrease	Decrease	Increase
C	Decrease	Increase	Decrease
D	Increase	Decrease	Increase
E	Increase	Increase	Decrease
F	Increase	Increase	Increase

14. 7-year-old female is brought to her pediatrician with complaint of lower back pain. The patient mentions that she has recently gone through a growth spurt of 4 cm (1.6 inches) and is now taller than all of the boys in her class. The pediatrician proceeds with a full examination, which reveals Tanner stage 3. In addition to these, which of the following developmental signs would this patient most likely show?
A. Coarse pubic hair and enlarged breasts
B. Coarse pubic hair and raised areola
C. Coarse pubic hair extending to medial thigh and flattened areola
D. Downy pubic hair and formation of the breast bud
E. Lack of pubic hair and flat chest with raised nipples
15. A young couple is trying to conceive their first child. A friend tells the woman that she should take her temperature daily to determine when she ovulates. The woman asks

her physician if this is true, and her physician explains that changes in the concentration of a particular hormone during ovulation lead to temperature changes. The action of which of the following hormones is responsible for this change in body temperature?
A. Estrogen
B. Follicle stimulating hormone
C. Human chorionic gonadotropin
D. Luteinizing hormone
E. Progesterone
16. A 56-yearold woman presents to her primary care physician for her yearly check up. During a discussion of her recent history, she states that she has been feeling well, except for some instances every few days over the past 2 months-when she feels very warm at night and needs to open her bedroom window to cool off, even in the middle of winter. She denies any cough and has no recent history of travel. In addition, she states that over the past year her vagina has been dry, and she has had to use lubricant before intercourse. Findings on speculum examination are unremarkable, except for the vaginal dryness. According to the table provided, which of the following is the most likely hormonal profile of this woman relative to a healthy 20-year-old woman?

Choice	Estrogen	LH	FSH	GnRH
A	↓	↓	↓	↑
B	↓	↓	↓	↓
C	↓	↑	↑	↑
D	↑	↑	↑	↑
E	↑	↑	↑	↓

17. A researcher is studying a hormone that is normally secreted from the pancreas during times of starvation. She creates a transgenic mouse with a knockout of this hormone s receptor to better study its signaling mechanisms. Which type of receptor is functioning abnormally in this knock-out mouse?
A. G-protein-coupled receptor
B. Intracellular steroid receptor
C. lon channel-linked receptor
D. Receptor serine/threonine kinase
E. Receptor tyrosine kinase
18. A researcher team is studying diabetes mellitus. The team is trying to understand the molecular pathways involved in insulin resistance. They create a strain of genetically altered mice witha mutated insulin receptor that is only partially activated upon ligand binding. Under normal cellular conditions, the insulin-receptor mediated signaling cascade is analogous to which of the following?
A. ACTH

B. BNP
C. Cortisol
D. Erythropoietin
E. IGF-1

19. A 42-year-old woman comes to the physician for the first time in years, complaining of frequent headaches for the past 6 months. Her pain is mild in intensity (4/10 on the pain scale). She also reports a recent increased need to urinate and increased thirst. The physician notes a broadening of her brow and protrusion of her jaw, which had not been present at previous visits. Pharmacologic treatment is initiated. Treatment for this patient's condition is most likely to directly inhibit the release of which of the following hormones?

A. ACTH
B. Cortisol
C. Insulin
D. Parathyroid hormone
E. Testosterone

20. A 28 year-old man is found in the mountains by a rescue team after becoming lost during a hike; he is transported to the nearest medical center. He is unable to provide any history but has not had access to food. He nauseated, delirious, and weak. He appears unkempt and confused and is visibly thin. In a state of hypoglycemia, which of following is most likely?

A. Beta cells will remain depolarized until energy requirements are met
B. Beta islet cells activity is increased
C. Decreased activation of voltage gated calcium channels in beta cells
D. Glucose will not enter beta islet cells
E. Oxidative metabolism is inhibited
F. Voltage-gated calcium channels will allow calcium to accumulate intracellularly

21. A 42-year-old woman presents to the office with complaints of excessive urination over the past few weeks. During this period, she has woken up on two occasions to urinate in the middle of the night. She says she has been taking lithium for 9 years to treat her bipolar disorder. She is compliant with her medication and denies any other complaints. Her blood pressure is 105/65 mm Hg and her heart rate is 78/min. A full blood and urine workup is initiated, which shows increased serum lithium levels, serum sodium of 155 mEq/L, and serum osmolality of 330 mOsm/L. The patient is further evaluated with a water deprivation test, which shows no change in her urine osmolality. The physician subsequently injects her with desmopressin, but her serum osmolality still doesn't change.

Which of the following urine osmolality values most closely reflects her condition?

A. 100 mOsm/kg

B. 290 mOsm/kg
C. 360 mOsm/kg
D. 425 mOsm/kg
E. 800 mOsm/kg
22. A 35-year-old man with controlled diabetes mellitus is enrolled in a clinical study examining the difference between serum glucose levels and urine glucose levels in patients with type 2 diabetes mellitus. As part of this study, the patient eats a large carbohydrate-rich meal and then has serial serum and urine glucose levels measured. Although his serum glucose level begins to rise rapidly, glucose only becomes detectable in his urine several hours later. Glucose does not become immediately detectable in his urine because of what feature of the nephron?
A. Impermeability of occluding proteins in the tight junctions of glomerular capillary endothelial cells
B. Kinetics of a sodium-dependent symporter in the distal convoluted tubule
C. Kinetics of a sodium-dependent symporter in the proximal convoluted tubule
D. Kinetics of a sodium-potassium exchange pump in the distal convoluted tubule
E. Kinetics of a sodium-potassium exchange pump in the proximal convoluted tubule
23. A researcher is designing an in vitro experimental system to study glucose transport into skeletal muscle. The system will measure the time course of uptake of radiolabeled 2- deoxyglucose in cultured cells both before and after the addition of insulin. Which of the following cell types utilize the same glucose transporter as skeletal muscle?
A. Adipocytes
B. Cortical neurons
C. Erythrocytes
D. Hepatocytes
E. Pancreatic B cells
24. Steroid hormones are unique in that they enter the cell and act directly on DNA to effect gene expression level changes, rather than acting only through intermediary signaling proteins. Which of the following steps immediately precedes steroid hormone-receptor complex binding to DNA?
A. Conformational change of the hormone-receptor complex
B. Hormone binding to a DNA enhancer element
C. Hormone binding to a hormone-specific globulin
D. Hormone binding to a membrane receptor
E. Hormone binding to its intracellular receptor
25. A 6-year-old girl is brought to the pediatrician's office by her mother, who is concerned that the child has started developing underarm hair, pubic hair, breasts, and body odor. The mother also mentions that her child is taller than most of her classmates. The patient and her mother deny vaginal bleeding. On examination, vital signs are

unremarkable. She is in the 95th percentile for height and weight. There are no abnormalities on neurologic examination, and no masses are palpated in the abdomen. Results of a complete metabolic profile are within normal limits. Which of the following mechanisms is most likely responsible for this patient's condition?

A. 21-hydroxylase deficiency
B. Constant G protein activation
C. Continuous stimulation of pituitary gonadotropic cells
D. Germinoma
E. Pulsatile stimulation of pituitary gonadotropic cells

26. An 8-year-old girl is brought for evaluation after her mother noticed some blood staining on the patient's underwear. The patient's mother states that t appears her daughter has started to develop breasts and is concermed that this is "happening too fast" because she is only 8 years old. The patient is otherwise healthy and takes no medications. Her vital signs are within normal limits. On physical examination, the patient is noted to have Tanner stage ll breast budding, pubic hair, and underarm hair. Which of the following is the most appropriate next step?

A. GnRH stimulation test
B. Hand and wrist x-ray
C. Hormonal analysis
D. MR
E. Pelvic Ultrasound
F. Reassurance

ANSWERS MCQs STEP 1

1. The correct answer is C. All of the choices listed are reactions that occur in the synthetic pathway from cholesterol to cortisol. ACTH stimulates the first reaction in the pathway: cholesterol to pregnenolone. This reaction is catalyzed by the enzyme cholesterol desmolase. The next step in the pathway is pregnenolone to progesterone (choice D); progesterone is then converted to 17-hydroxyprogesterone (choice E); 17-hydroxyprogesterone is converted to 11-deoxycortisol (choice B) by the enzyme 21 beta-hydroxylase; and the 11-deoxycortisol is then converted to cortisol (choice A).

2. The correct answer is C. This question requires you to equate salt restriction with an increased synthesis of aldosterone (aldosterone promotes sodium reabsorption) and then to remember that aldosterone is produced in the zona glomerulosa of the adrenal cortex. The zona glomerulosa is the outermost layer of the adrenal cortex.

The adrenal medulla (choice A) secretes catecholamines.

The zona fasciculata (choice B) is the middle layer of the adrenal cortex. It primarily secretes glucocorticoids.

The zona reticularis (choice D) is the innermost layer of the adrenal cortex. It primarily secretes

androgens such as dehydroepiandrosterone (DHEA).

3. The correct answer is A. Addison disease, or primary adrenal insufficiency, is caused by destruction of adrenal cortical tissue. As a consequence of the loss of mineralocorticoids, there is reduced ability to retain sodium and excrete potassium. (Recall that aldosterone acts on the renal collecting duct to promote resorption of Na+ and secretion of K+.) Hence, this patient has hyponatremia and hyperkalemia. Low plasma sodium is accompanied by hypovolemia, signs of dehydration, and hypotension.

Hyperaldosteronism (choice C), in contrast with the hypoaldosteronism of Addison disease, is accompanied by hypokalemia and hypertension.

Diabetes insipidus (choice B) is the consequence of a lack of sufficient ADH. The ensuing loss of urinary water also can result in hypernatremia.

Psychogenic polydipsia (choice D) can produce hyponatremia. However, the outcome of excessive drinking of water would not be signs of dehydration or hypotension.

In the syndrome of inappropriate ADH secretion (SIADH) (choice E), ADH is secreted and water is retained. SIADH also produces hyponatremia without signs of hypovolemia or dehydration.

4. The answer is C. Excess aldosterone secretion may be due to an abnormality of the adrenal gland (primary aldosteronism) or an abnormality of excess renin secretion (secondary aldosteronism). Causes of primary hyperaldosteronism (Conn's syndrome), which is independent of the renin-angiotensin-aldosterone (RAA) system, include adrenal cortical adenomas (most commonly), hyperplastic adrenal glands, and adrenal

cortical carcinomas. These diseases are associated with decreased levels of renin. The signs of primary hyperaldosteronism include weakness, hypertension, polydipsia, and polyuria. The underlying physiologic abnormalities include increased serum sodium and decreased serum potassium, the latter due to excessive potassium loss by the kidneys, which together with the loss of hydrogen ions produces a hypokalemic alkalosis. The elevated level of serum sodium causes expansion of the intravascular volume. In contrast to Conn's syndrome, secondary hyperaldosteronism results from conditions causing increased levels of renin, such as renal ischemia, edematous states, and Bartter's syndrome. Causes of renal ischemia include renal artery stenosis and malignant nephrosclerosis, while Bartter's syndrome results from renal juxtaglomerular cell hyperplasia.

5. The correct is D. Tuberculosis is known to increase the susceptibility of developing chronic adrenal insufficiency, also known as hypocortisolism, or Addison disease. It leads to hyperpigmentation as seen in the palmar skin creases and nails of the woman. Administration of cortisol replaces the inadequate release of glandular cortisol. Cortisol decreases protein synthesis and increases protein degradation. The newly available amino acids are then used for gluconeogenesis, which lead to the name "glucocorticoid" for cortisol. Increasing serum cortisol levels will decrease, not increase, secretion of ACTH (choice A) and CRH (choice B) by feedback inhibition. Cortisol decreases, not increases, the sensitivity of cells to insulin (choice C) by decreasing the translocation of glucose transporters to the cell membrane. Because cortisol decreases utilization of glucose by muscle and adipose tissue, blood glucose rises. This provides a stimulus to release insulin. Thus, prolonged exposure to high levels of cortisol can lead to diabetes mellitus due to exhaustion of pancreatic beta cells. Although cortisol acts as an anti-inflammatory agent, it has a negative, not a positive, effect on wound healing (choice E). Cortisol suppresses the activity of leukocytes which are important for debriding the wound. Cortisol increases catabolism, which leads to the breakdown of nutrients that are needed for generating new tissue. Cortisol stimulates catecholamines leading to vasoconstriction and consequent reduction of oxygen, nutrient, and white blood cell delivery. Cortisol may also inhibit collagen production.

6. The correct is D. In the adrenogenital syndrome, the failure to make cortisol due to lack of the adrenal enzyme 21-β-hydroxylase results in an inability to provide negative feedback suppression of ACTH production. As a result, the adrenal glands are under constant stimulation to maximize steroidogenesis. Substrates that cannot reach cortisol flow down other pathways and by mass action drive the massive overproduction of androgens, which can also be peripherally aromatized to estrogens. No significant change in serum cholesterol is observed (choice E), probably because the cholesterol reservoir in the body is large, even compared to the massive levels of

steroids being synthesized in this syndrome. Cortical atrophy (choice A) and release of excess cortisol (choice C) are the opposite of what is observed. There is no mechanism to achieve selective hypertrophy of the adrenal medulla (choice B) because the action of ACTH to drive adrenal hypertrophy is limited to the cortex.

7. The correct answer is D. During menopause, there is a loss of functioning follicles in the ovaries such that GnRH-stimulated LH and FSH secretion do not result in normal estrogen secretion. The low estrogen levels cannot inhibit gonadotropin secretion in a negative-feedback fashion, resulting in very high levels of LH and FSH.

Choices A, B, C, and E do not accurately describe normal hormonal levels in menopause.

8. The correct answer is A. Estrogen levels peak at the end of the follicular phase of the menstrual cycle, creating positive feedback to the hypothalamus and pituitary gland. This increases the number of GnRH spikes per 24 hours, causing a surge of both follicle-stimulating hormone (FSH) and luteinizing hormone (LH). It is the surge of LH, in combination with the high estrogen levels, that induces ovulation.

FSH levels (choice B) peak at ovulation.

Gonadotropin-releasing hormone (choice C) is released in pulses, not in a continuous pattern as is estrogen.

LH levels (choice D) peak at ovulation.

Progesterone (choice E) peaks during the premenstrual phase of the cycle. It is represented by the solid line on the graph.

9. The correct is E. Although the early maturation of an ovarian follicle depends on the presence of FSH, ovulation is induced by a surge of LH. Although estrogens (choices Aand B) usually have a negative feedback effect on LH and FSH secretion, the LH surge seems to be a response to elevated estrogen levels. In concert with FSH, LH induces rapid follicular swelling. LH also acts directly on the granulosa cells, causing them to decrease estrogen production, as well as initiating production of small amounts of progesterone. These changes lead to ovulation. FSH (choice C) causes follicle maturation, and is also required for Sertoli cells to mediate the development of spermatids into mature sperm cells. Inhibin (choice D) is a polypeptide secreted by the testes and ovaries that inhibits FSH secretion.

10. The correct is D. It represents the estrogen estradiol, which is produced from androgen by granulosa cells of the ovaries and released into the capillaries. A woman's estradiol serum concentration roughly reflects the activities of her ovaries. Estradiol levels rise during the follicular phase of the menstrual cycle (days 0–13). They reach peak levels shortly before ovulation on day 13–14, and drop back during the luteal phase (days 14–28). They reach menstrual/follicular levels at the end of the luteal phase unless there is a pregnancy. After menopause, the ovaries atrophy and estradiol levels become very low. During reproductive cycles, androgens are the main substrate for

estrogen synthesis in the granulosa cells. The androgen-estrogen conversion is under the influence of FSH (choice E). FSH concentrations are high after menopause compared to their premenopausal concentrations. The source of androgens is theca cells. They produce it from cholesterol under the influence of LH (choice B). LH concentrations, like FSH, are high postmenopausal. Both, FSH and LH levels are used as a diagnostic tool to determine menopause. Granulosa cells also produce progesterone (choice C) from cholesterol. Progesterone serum levels are low during follicular phase of the menstrual cycle and high during the luteal phase of the menstrual cycle. The transition of cholesterol to progesterone is under the influence of LH (choice A).

11. The correct answer is E. Glucagon is released from the alpha cells of the pancreas in response to hypoglycemia and stimulates glycogenolysis to increase serum glucose. Augmented calcium deposition in bone (choice A) is achieved by calcitonin (inhibits bone resorption), which is secreted by the C-cells in the thyroid gland. Glucagon plays no role in calcium metabolism.

Glucagon favors the conversion of amino acids to glucose (gluconeogenesis) rather than their storage in the liver (choice B).

Insulin (which generally has opposite effects of glucagon) promotes lipogenesis in the liver and in adipose tissue (choice C).

Glucagon stimulates gluconeogenesis (choice D).

12. The answer is E. The islets of Langerhans, which constitute 1 to 2% of the pancreatic weight, secrete insulin, glucagon, somatostatin, and pancreatic polypeptide. Each is secreted from a distinct cell type, A, B, D, and F, respectively. The islets are scattered throughout the pancreas, but are more plentiful in the tail than in the body or head.

13. The correct answer is D. The disease is acromegaly, which is typically produced by a growth hormonesecreting pituitary adenoma. Growth hormone synthesis is predominately regulated by hypothalamic GHRH (growth hormone releasing hormone), and its pulsatile secretion is predominately regulated by hypothalamic somatostatin.

Choice A: Dopamine and norepinephrine are catecholamines that regulate smooth muscle tone and cardiac function.

Choice B: Luteinizing hormone (LH) regulates sex steroid hormone production by both testes and ovaries. Human chorionic gonadotropin (hCG) is produced by the placenta and has actions similar to LH.

Choice C: Prolactin regulates menstruation and lactation. Follicle stimulating hormone (FSH) regulates ovarian and testicular function.

Choice E: Thyroid stimulating hormone (TSH) regulates secretion of thyroid hormones. Adrenocorticotropin (ACTH) regulates glucocorticoid and adrenal androgen secretion.

14. The correct answer is C. Atrial stretch results in secretion of atrial natriuretic factor (ANF), a polypeptide hormone that increases urinary sodium excretion and therefore decreases intravascular volume to maintain homeostasis. None of the remaining answer choices are appropriate physiologic responses to increased atrial filling. Aldosterone (choice A) causes sodium retention by increasing sodium and water reabsorption in the distal convoluted tubule. This leads to an increased intravascular volume.

Activation of atrial baroreceptors results in increased secretion of ADH (choice B), a polypeptide hormone that decreases urine concentration and increases intravascular volume.

Norepinephrine (choice D) causes vasoconstriction and increased blood pressure, which can produce a reflex decrease in heart rate.

Renin (choice E) converts angiotensin I to angiotensin II, a potent vasoconstrictor that stimulates aldosterone secretion from the adrenal cortex, resulting in increased intravascular volume.

15. The correct is B. ADH acts to increase renal water conservation secondary to dehydration. Choice B, which can result from dehydration, is the logical trigger for ADH secretion. Angiotensinogen (choice A) is inactive and will not directly stimulate ADH, but its active metabolite angiotensin II or III will increase ADH secretion. Choices C, D, and E will either inhibit, or have minimal effects on ADH secretion.

16. The correct is E. Excessive vomiting can lead to large losses in fluid and electrolytes. Dehydration triggers the sense of thirst. Her age, her extremely low body mass index (normal 18.5–24.9), and her frequent vomiting all point toward anorexia nervosa. Anorexic people might drink large amounts of water to reach target weight. By drinking a lot of water without adequately replacing electrolyte imbalances, water intoxication can result. Diluted serum sodium levels can lead to headaches and seizures. Although vomiting, weight loss, and fainting due to low blood pressure could point toward Addison disease, the typical symptoms of hypocortisolism, which include hyperkalemia, hyperosmolality, and hyperpigmentation, are not mentioned and hence make choice A not the best one. In patients with diabetes insipidus, whether caused by a lack of ADH (choice B) or by failure of the kidney to adequately respond to ADH (choice D), serum osmolality is expected to be high. Normal glucose values make uncontrolled diabetes mellitus not the best working diagnosis (choice C).

17. The correct is D. High-dose exogenous glucocorticoids suppress the adrenal neuroendocrine axis. Patients treated for longer than 2 weeks need to be tapered off glucocorticoids slowly to avoid adrenal insufficiency. Other complications of high-dose glucocorticoids include growth suppression, not excessive growth (choice A) in children and volume overload, not volume depletion (choice E). Hyperkalemia (choice

B) and hyponatremia (choice C) are observed in adrenal insufficiency due to loss of mineralocorticoid effects and are not relevant to glucocorticoid therapy.

18. The correct is B. The accident trauma produces extensive loss of fluid from the vasculature into the interstitial fluid space. Hence venous return to the heart, and thus left atrial pressure will be reduced. The decrease in arterial pressure will trigger arterial baroreflexes which will activate the sympathetic nervous system and increase catecholamine release (choice A). Likewise the fall in pressure will cause increased renin/angiotensin/ aldosterone (choices C and E). Finally, the reduced perfusion of the tissues will generate increased lactate formation (choice D).

19. The correct is C. The primary control over prolactin secretion is inhibition by hypothalamic dopamine; all other anterior pituitary hormones are primarily controlled by hypothalamic hormone stimulation. Hence, with stalk transection, loss of connection of the hypothalamus to the pituitary is associated with decreased secretion of all pituitary hormones except prolactin, the secretion of which increases in the absence of dopamine. Secretion of growth hormone (choice B), proopiomelanocortin (choice D), and thyroid-stimulating hormone (choice E) all decrease. Gonadotropinreleasing hormone (choice A) is a hypothalamic hormone, and is not made in the pituitary gland.

20. The correct is D. The symptoms are consistent with acromegaly. It is a rare disease resulting from chronic exposure to growth hormone in adulthood and presents with elevated serum growth hormone levels and elevated serum IGF-1 levels. One treatment option for acromegaly is medication with somatostatin-analogues. These synthetic forms have a longer half-life than the normal polypeptide hormone, which is also called somatotropin release inhibiting factor (SRIF). Growth hormone (choice B), growth hormone-stimulating factors such as GHRH (choice A), and thyroid hormones (choice E) are incorrect treatments. Insulin (choice C) increases bone formation and the calcium content of bone and is therefore not part of the treatment. This can easily be remembered since insulin-like growth factor 1 (IGF-1) is an important stimulator of childhood growth.

21. The correct is C. Normally, an elevated plasma osmolarity will stimulate increased ADH secretion and cause increased renal water reabsorption, which should lower the elevated plasma osmolarity. Since in this case ADH is reduced in the face of elevated osmolarity and the kidney is not reabsorbing water, it is clear that neurogenic diabetes insipidus is present (choice C). Choice Ais incorrect because congestive heart failure will trigger water retention via the reduced cardiac output and lower arterial pressure, which stimulates ADH release via arterial baroreceptors. Choice B is incorrect because nephrogenic diabetes insipidus results from renal insensitivity to normal, or elevated circulating ADH levels. Choice D is incorrect because primary polydipsia is associated with reduced plasma osmolarity which will suppress ADH release. Choice E is incorrect because diabetes mellitus will be associated with elevated plasma and urine glucose levels.

ANSWERS MCQs IFOM

1. The correct answer is A. Pheochromocytoma is a rare tumor of the adrenal gland that secretes catecholamines (epinephrine and norepinephrine) in response to sympathetic stimulation. The adrenal medulla is innervated directly by the sympathetic nervous system, causing the release of catecholamines. The adrenal medulla is a unique sympathetic organ in that the nerves that supply it do not first synapse in other sympathetic ganglia. Presynaptic neurons in sympathetic ganglia use acetylcholine as their neurotransmitter, which in this case binds to nicotinic acetylcholine receptors in the adrenal medulla. The injection of high-potency acetylcholine would theoretically lead to an excess release of catecholamines from the adrenal medulla.

Epinephrine is a catecholamine secreted by the adrenal gland in response to sympathetic stimulation. It is the hormone released by this stimulation, rather than the molecule, that would lead to release.

Norepinephrine is a catecholamine secreted by the adrenal gland in response to sympathetic stimulation. It is the hormone released by this stimulation, rather than the molecule, that would lead to release.

Dopamine is a molecule secreted by the adrenal medullary cell. However, it does not stimulate adrenal medullary secretions.

Cortisol is a steroid hormone produced in the adrenal zona fasciculata. The release of corticotropin-releasing hormone from the hypothalamus, followed by the release of ACTH from the pituitary, leads to cortisol production.

2. The correct is D. This female patient presents with primary amenorrhea, hypertension, and low potassium. She is diagnosed with a congenital adrenal hyperplasia disorder. From her clinical presentation, we can deduce that she has a 17a-hydroxylase deficiency, which would lead to overproduction of mineralocorticoids secreted from the zona glomerulosa.

17a-Hydroxylase deficiency is characterized by deficits in glucocorticoid and sex steroid synthesis and increased mineralocorticoid synthesis. The increased levels of mineralocorticoids lead to increased sodium retention and potassium excretion, which explains this patient's hypertension and hypokalemia. The low levels of sex steroids clinically manifest in a female with no sexual maturation. This is seen in our patient, who has primary amenorrhea and a lack of secondary sexual characteristics such as Tanner stage 1 breasts. Males with 17a-hydroxylase present with ambiguous genitalia and undescended testes.

Mineralocorticoids are produced in the zona glomerulosa, and their synthesis requires 21-hydroxylase and 11B-hydroxylase, but not 17a-hydroxylase. 17a-Hydroxylase is the only congenital adrenal hyperplasia that manifests with decreased sex hormones,

as 17a-hydroxylase is the enzyme needed for the pathway of sex steroid hormone synthesis.

21-Hydroxylase deficiency manifests with hypotension, hyperkalemia, and continued production of sex hormones leading to virilization in females. It the most common congenital adrenal deficiency and manifests in infancy with salt- wasting or in childhood as precocious puberty. An 11β-hydroxylase deficiency manifests with hypertension, hypokalemia, and virilization in females. By closely paying attention the patient's blood pressure, labs, and sexual characteristics, you can differentiate among the causes of congenital ad renal hyperplasia.

Sex steroid hormones are produced in the zona reticularis. Continued production of sex steroid hormones is seen in both 21-hydroxylase and 18-hydroxylase deficiency.

The medulla produces the catecholamines, epinephrine and norepinephrine, which are amine hormones. Overproduction of catecholamines would manifest with with, hypertension, headaches, palpitations, flushing, and sweating. This patient's clinical presentation of hypertension, hypokalemia, and lack of sexual maturation is not indicative of defects in catecholamine synthesis.

An excess of cortisol, which is produced in the zona fasciculata of the adrenal cortex, would lead to Cushing syndrome. Cushing syndrome manifests with hypertension, weight gain with central obesity, fatigue, skin thinning, and psychological disturbances (depression, anxiety).. Excess cortisol production would not lead to a lack of sexual maturation.

The capsule does not produce any hormones and is not responsible for any of the symptoms described in this clinical vignette.

Remember the mnemonic "Salt, Sugar, and Sex" for the layers of the adrenal cortex and their respective products, with "salt" corresponding to the outer zona glomerulosa, "sugar" corresponding to the middle zona fasciculata, and "sex" coresponding to the inner zona reticularis.

3. The correct answer is B. This patient is a 21-year-old healthy woman who is sexually active and desires oral contraceptive pills (OCPs). She has no contraindications (relative or absolute) to combination OCPs (no personal or family history of thromboembolic disease, normal blood pressure, nonsmoker). After a discussion about all forms of contraception, the physician decides to prescribe the combination OCPs the patient desires. To understand the mechanism of action of OCPs, it is helpful to understand the hormonal changes that occur in the normal menstrual cycle. The normal menstrual cycle consists of the follicular phase (usually 14-21 days) and the luteal phase (14 days) The follicular phase begins after the onset of menstruation and is characterized by FSH-stimulated growth of one or more dominant follicles that release estrogen. Estrogen causes the uterine endometrium to enter the follicular phase, which is characterized by a thickened endometrium with an

increased number of glands. For most of the follicular phase, estrogen also works to exert negative feedback on FSH and luteinizing hormone (LH) production, but late in the follicular phase, high serum estrogen begins to have a positive feedback effect on LH production, leading to the LH surge (a 10-fold increase in the serum LH concentration). The LH surge characterizes the start of the luteal phase and subsequent ovulation. The oocyte of the dominant follicle completes its first meiotic division and is released from the follicle-36 hours after the LH surge. The remnant follicle becomes the corpus luteum, which releases progesterone in the mid to late luteal phase. Progesterone causes the endometrium to cease thickening and causes glands to "organize" ("'secretory endometrium"). The corpus luteum begins to resolve in the late luteal phase, which occurs when LH release declines via negative feedback mechanisms from the rising serum progesterone concentration. As the corpus luteum resolves, serum concentrations of progesterone and estrogen decrease, resulting in loss of endometrial blood supply, endometrial sloughing, and the onset of menses. Standard combined OCPs consist of progesterone and estrogen. Progesterone provides negative feedback to decrease the release of gonadotropin-releasing hormone from the hypothalamus, which then decreases the secretion of FSH and LH by the anterior pituitary. The immediate effect of decreased FSH is to inhibit follicular development and to prevrent the increase in estrogen concentration during the fallicular phase. Without the end- follicular peak in estrogen concentration, positive feed back with LH release cannot occur, and thus the LH surge cannot happen. Without the LH surge, ovulation cannot occur.

The incorrect answers are wrong for the following reasons:

Although the decreased concentration of FSH leads to the downstream effect of ovulation inhibition, ovulation is not the process that is most immediately and directly affected by the decrease in the FSH concentration. A decreased FSH concentration leads to a decreased follicular-phase estrogen concentration, which prevents the LH surge and subsequent ovulation.

It is only by way of a decreased estrogen concentration that a decreased FSH concentration serves to prevent the LH surge. Specifically, a decreased FSH concentration leads to a decreased follicular-phase estrogen concentration, which prevents the LH surge and subsequent ovulation.

OCPs decrease the FSH concentration, which prevents fertilization only indirectly by way of ovulation inhibition because fertilization cannot occur in the absence of an ovum. Unlike OCPs, intrauterine contraceptive devices (IUDs) work primarily by inhibiting fertilization. Progesterone released from hormonal IUDs thickens the cervical mucus to prevent sperm from reaching the fallopian tube. Copper lUDs contain copper ions that act as spermicide, which prevents sperm from fertilizing the ovum.

During the luteal phase of the menstrual cycle, progesterone acts to prepare the endometrium for blastocyst implantation via the formation fertilizing the ovum.
Secretory endometrium is characterized by organization of the endometrial glands, intertwining of the endometrial glands with the arteries, and edematous endometrial stroma. Copper IUDs may work to prevent implantation of the blastocyst.

4. The correct is C. The husband has clinical findings of tall height, oligospermia, small and firm testes, and sparse body hair, which are highly suggestive of Klinefelter syndrome, the most common cause of male hypogonadism, occurring in 1 out of 1000 live male births. Klinefelter syndrome is most commonly caused by a meiotic nondisjunction event during parental gametogenesis that results in an extra X chromosome, leading to the 47,XXY karyotype in men (shown in the image). This extra X chromosome is responsible for the clinical manifestation in these patients. Primary hypogonadism is the cardinal feature. Phenotypic findings include azoospermia (absence of sperm in semen), small/firm testes, absent secondary male characteristics (including deep voice, beard, and male pattern pubic hair), and tall stature.

These patients typically have primary testicular failure due to the abnormal Leydig cell function (resulting in low testosterone levels) and a progressive destruction and hyalinization of the seminiferous tubules (resulting in low serum inhibin levels). This leads to small, firm testes and oligospermia or azoospermia. A decrease in testosterone levels and inhibin B levels results in excess gonadotropins (increased luteinizing hormone level and follicle-stimulating hormone level) due to loss of feedback inhibition. Excess gonadotropins stimulate aromatase activity, which in turn increases estrogen levels, causing gynecomastia. These patients are often taller than their peers and may present with:

Long extremities (due to testosterone deficiency)
Distribution patterns of fat and hair more typical of women
Psychosocial issues

Testicular dysfunction and the lack of negative feedback leads to an abnormal hypothalamic-pituitary-gonadal axis, which explains many of the components of this syndrome such as infertility, eunuchoid habitus, and gynecomastia. Patients may not be diagnosed until late in life when they present with infertility due to hypogonadism.
Decreased follicle-stimulating hormone levels may be seen in patients with prolactinoma. High prolactin levels inhibit gonadotropin-releasing hormone, which which subsequently decreases the secretion of both FSH and LH.
Decreased gonadotropin-releasing hormone levels are seen in Kallmann syndrome, which is characterized by delayed or absent puberty and an impaired sense of smell (anosmia). It occurs due to defective migration of GnRH-releasing neurons to their

anatomic location in the hypothalamus, leading to reduced synthesis of GnRH and reduced levels of gonadotropins and testosterone.

Normal follicle-stimulating hormone levels in a patient lacking in sperm may have an obstruction somewhere along the path from the testes to the seminal fluid. For example, this condition occurs in men with cystic fibrosis, who have congenital absence of the vas deferens.

5. The correct answer is B. This patient is a 33 year-old man with history of attention-deficit hyperactivity disorder and cryptorchidism who presents with infertility. He is found to have gynecomastia, minimal body hair, long extremities, small firm testes, and elevated FSH and LH levels. Overall, presentation is concerning for hypergonadotropic hypogonadism caused by Klinefelter syndrome.

Most patients with Klinefelter syndrome are of 47, Y genotype. Klinefelter syndrome is the most common congenital abnormality causing primary hypogonadism and results from nondisjunction of the sex chromosomes of either parent during meiotic division. The major clinical manifestations of Kinefelter syndrome include tall sature, small testes, and infertility (azoospermia) that become noticeable after puberty. Patients with Klinefelter syndrome are at increased risk for psychiatric disorders, autism spectrum disorders, and social problems.

An image of the hypothalamic-pituitary-gonadal axis in a typical 46,XY male is provided. Pulsatile gonadotropin-releasing hormone (GnRH) secretion from the hypothalamus stimulates the release of FSH and LH from the anterior pituitary. LH then stimulates the Leydig cells of the testes to release testosterone, and FSH stimulates the Sertoli cells of the testes to release inhibin B. Testosterone then feeds back to the hypothalamus and anterior pituitary, where it negatively regulates GnRH and LH, respectively. Inhibin B feeds back to the anterior pituitary, where it suppresses FSH secretion.

Individuals with Klinefelter syndrome have dysgenesis of the seminiferous tubules and therefore have decreased numbers of the Sertoli cells and developing sperm cells. With decreased Sertoli cells, a lesser amount of inhibin B is produced, and there is decreased negative feed back of FSH release at the level of the anterior pituitary. Therefore individuals with Klinefelter syndrome have high FSH levels. The incorrect answers would not directly explain this individual's increased FSH levels. Leydig cells are the interstitial cells of the testicle that produce testosterone. Abnormal Leydig cell function is also usually present in patients with Klinefelter syndrome. Individuals with Klinefelter syndrome therefore have decreased levels of testosterone. Less testosterone is available to negatively regulate GnRH release from the hypothalamus and LH release from the anterior pituitary. Inactive cells in the interstitium of the testicles and low levels of testosterone would explain this individual's increased LH levels but not his increased FSH.

Any individual with two X chromosomes (eg, a 46,XX female or a 47,XXY male) has an inactivated X chromosome on karyotype (a Barr body). This inactivated X chromosome does not affect FSH production.

6. The correct answer is D. This patient is a 52-year-old woman who presents with amenorrhea (last menstrual period was 12 months ago) and hot flashes (heat with sweating and rapid heartbeat). Examination reveals decreased vaginal rugae and dryness. These are classic symptoms of menopause, which in the United States commonly occurs around age 51. Menopause is the cessation of estrogen production secondary to the age-linked decline in the number of ovarian follicles. Complications of menopause include hot flashes, vaginal atrophy, and osteoporosis (all due to decreasing levels of estrogen), as well as an increased risk of coronary artery disease. HRT increases bone mineral density and decreases the risk of osteoporotic fractures; the mechanism of decreased bone loss is estrogen's inhibition of osteoclastic bone resorption. However, it should be noted that HRT has serious adverse effects. HRT actually increases, rather than decreases, the risk of stroke and myocardial infarction. Before the Women's Health Initiative trial, many women were given HRT to relieve the symptoms of menopause because it was thought to decrease cardiovascular risk. However, the trial results demonstrated many serious negative outcomes from estrogen-progestin HRT, including increased incidence of invasive breast cancer. However, in recent years, many of the conclusions of the Women's Health Initative trial have been questioned. Recommendations regarding HRT are continually evoving and unresolved debate surrounds many of the proposed risks that have been thought to be associated with HRT. Nonetheless, HRT is a well-established and efficacious treatment for symptomatic perimenopause. Cervical cancer is associated mainly with HPV, and HRT or hormone therapy does not directly affect the risk of cervical cancer. Moreover, menopause itself is not associated with an increased risk of cervical carcinoma. Similarly, the risk of uterine cancer is unchanged by HRT, since HRT involves a combination of estrogen and progestin.

7. The correct answer is B. This 18-year old patient presenting with amenorrhea for 6 months has an elevated BMI (31), elevated testosterone, and increased LH:FSH ratio which strongly suggests polycystic ovarian syndrome (PCOS). This disease often has onset during the late teenage years to early 20s. Patients will often also report hirsutism and deepening voice. Ultrasound typically shows multiple cysts in the ovaries, however, the presence of cysts is not necessary to make the diagnosis. PCOS is a hyperandrogenic state in which high levels of testosterone cause most of the clinical signs. The small anovulatory follicular cysts secrete large amounts of estrogen as well, at levels high enough to have positive feedback on luteinizing hormone (LH) release. However, the high estrogen levels inhibit follicle-stimulating hormone (FSH) release. None of the follicles that develop in these ovaries are mature so LH is unable to induce

ovulation. Therefore in PCOS, a patient would have elevated testosterone, estrogen, and LH levels, with low FSH levels. Also key would be an elevated LH:FSH ratio, which is also seen in PCOS. Complications include type 2 diabetes and metabolic syndrome, thus, physicians need to test glucose levels to monitor for insulin resistance and associated complications.

The other answer choices would not be affected in PCOS. B-Human chorionic gonadotropin would indicate pregnancy but LH and FSH are typically low in pregnancy. Cancer antigen 125 would be useful for monitoring ovarian cancer treatment but ovarian cancer would be highly unlikely in this patient due to her age. Increased prolactin levels are not cross-interact with testosterone so the physical changes seen in PCOS would not be seen. Changes in thyroid-stimulating hormone, triiodothyronine, and thyroxine levels are associated with thyroid issues, most likely hypothyroidism, would present with additional symptoms beyond amenorrhea alone.

8. The correct answer is C. The patient with hypertension, proteinuria, and signs of end-organ damage (headache and blurry vision) likely has preeclampsta, and magnesium toxicity has resulted from her treatment. Preeclampsia is treated with magnesium to lower blood pressure and prevent seizures (progression to eclampsia). Magnesium sulfate is the drug of choice for preventing seizures in women with preeclampsia during labor and is given in very high doses. Loss of deep tendon reflexes (hyporeflexia) is one of the first signs of toxicity (magnesium level= 4.0-5.0 mmol/L), along with central nervous system depression (drowsiness) and flushing. Respiratory depression, coma, and eventually cardiac arest can occur at higher magnesium levels.

Hypermagnesemia does not cause hyperactivity, hypertension, or involuntary movements. Magnesium also does not cause a rash, although many anti seizure agents, such as carbamazepine and phenytoin, carry the risk of Stevens-Johnson syndrome, which is characterized by bullae formation with a fever. Note that any drug allergy can cause a rash. Phenytoin can cause nystagmus, and it is used to treat epilepsy, not to prevent eclampsia.

9. The correct answer is E. This woman is in the secretory (also called luteal) phase of her menstrual cycle, which occurs after ovulation (approximately day 14 of a typical menstrual cycle) through the end of the cycle. Progesterone increases after ovulation (as it is produced by the corpus luteum) and usually peaks around day 21-22. Progesterone is responsible for the increased endometrial production of glycogen and the differentiation and maintenance of the endometrium. The estrogen level is high just prior to ovulation (t induces the LH peak), but falls dramatically around the time of ovulation (when the follicle becomes the corpus luteum). After ovulation, the estrogen levels begin to rise again, returning to a relative peak during the luteal phase (around day 21). The high levels of estrogen and progesterone act in negative feedback during the luteal phase, inhibiting the release of FSH and LH, therefore during the secretory

phase, progesterone and estrogen levels are high and FSH and LH levels are low due to negative feedback.

Choice A represents a combination of hormone changes seen during the end of the menstrual cycle, when the corpus luteum degenerates. This woman is on day 19 of her cycle and, thus, still has a corpus luteum.

Answer B is characteristic of the follicular phase of the menstrual cycle, during which estrogen increases slowly due to the maturation of the follicle(s) under the influence of FSH This woman is in the secretory, or luteal, phase of her cycle, not follicular.

Answer C predominates in the days prior to ovulation. Progesterone levels remain low and stable, due to the lack of a corpus luteum, which is responsible for the secretion of the hormone later in the cycle.

Choice D is seen immediately following ovulation, when estrogen levels are decreasing (prior to increasing again duning the luteal phase) and progesterone levels are increasing (since the hormone is secreted by the newly formed corpus luteum).

10. The correct is A. The physician has likely ordering a pregnancy test that measures the amount of β human chorionic gonadotropin (β-hCG). Structuraly, β-hCG shares the identical a subunit as thyroid-stimulating hormone (TSH), luteinizing hormone (LH), and follicle-stimulating hormone (FSH). LH promotes rupture of the ovarian follicle during ovulation. Given the identical a subunit, the β subunit confers specificity to LH, FSH, TSH, and B-hCG. These hormones (except B-hCG) are secreted from the anterior pituitary gland. β-hCG is secreted by the syncytiotrophoblasts after fertilization.

None of the distractors list hormones that contain an α subunit identical to β-hCG. The hormone that promotes the release of cortisol and thyroid-stimulating hormone (TSH) are adrenocorticotropic hormone (ACTH) and thyroid-releasing hormone (TRH), respectively. The hormone that stimulates milk production is prolactin, and the hormone that stimulates uterine contractions during labor is oxytocin.

11. The correct is B. This woman is 15 weeks pregnant, and her physician is able to tell her the sex of her baby based on ultrasound findings. Dihydrotestosterone (DHT) is produced from testosterone by the enzyme 5a-reductase. It is three times more potent than testosterone. Prenatally, DHT is responsible for the formation of male external genitalia. Later, it is involved in the development of secondary sexual characteristics such as hair distribution, increased stature, and increased sweat gland secretion. DHT also causes an increase in the size of the epididymis and prostate.

Androstenedione is a weak androgen that does not significantly contribute to male external genitalia development. Testosterone itself is involved in male internal genitalia development. FSH and progesterone are not involved in the formation of external genitalia.

12. The correct answer is A. This is a 53-year-old female who hasn't menstruated in a year and says before that she often went 2-3 months without a period. She is also

experiencing periods of intermittent heat intolerance. Her estrogen level is low (s100 pg/mL), and levels of follicle-stimulating hormone (FSH), and luteinizing hormone (LH) are elevated. These laboratory results indicate that she is in menopause. The average age at onset of menopause is 51, and it is usually preceded by 4-5 years of irregular periods. Menopause is clinically defined as the cessation of estrogen production caused by a loss of ovarian sensitivity to gonadotropin stimulation due to ovarian dysfunction and a decreased number of available ovarian follicles. The acronym HAVOCS is used in describing the symptoms of menopause: Hot flashes, Atrophy of the Vagina, Osteoporosis, Coronaryartery disease (CAD), and Sleep disturbances.

Estrogen is necessary for the maintenance and development of the vagina and bone deposition, so a decrease leads to vaginal atrophy and osteoporosis.

The gonadotropins FSH and LH are elevated in menopause because of decreased feedback inhibition from estrogen on the anterior pituitary, but these levels are not the primary cause of menopause.

Decreased TSH is seen in hyperthyroidism. Though the patient is experiencing heat intolerance, it is intermittent and not consistent with hyperthyroidism. Nor is she presenting with other symptoms of hyperthyroidism, such as weight loss, increased heart rate, and possible palpitations.

Increased progesterone levels would lead to different symptoms, including depression, fatigue, and vaginal dryness. Increased testosterone is characteristic congenital adrenal hyperplasia or polycystic ovarian syndrome and would lead to masculine features such as hirsutism. In menopause, neither progesterone nor testosterone levels would be increased.

13. The correct answer is E. This 48-year-old patient presents with "hot flashes" and vaginal dryness that are highly suggestive of the changes seen as the result of menopause. Menopause is defined as 12 months of amenorthea that results from hormonal changes caused by ovarian follicle depletion. Because of a lack of a maturing follicle, there is decreased estrogen production and secretion. Normally, estrogen feeds back to the pituitary gland to decrease follicle-stimulating hormone (FSH) and luteinizing hormone (LH). Estrogen also feeds back to the hypothalamus, causing a decrease in gonadotropin-releasing hormone Without estrogen, there is a decrease in the negative feedback. Thus FSH and LH levels increase in the absence of sufficient estrogen to suppress them. A patient undergoing menopause will present with high FSH and LH levels along with a low estrogen level. The same patient would be expected to have a record of significantly different levels of each of these hormones from tests performed 10 years earlier (before entering menopause). Symptoms of menopause include vasomotor symptoms (hot flashes), sleep disturbance, mood disturbance, vaginal dryness, and dyspareunia. Estrogen (or combined hormone)

replacement therapy is a treatment option for women with menopausal symptoms. However, owing to potential adverse effects, these agents should be used at the lowest dose and for the shortest duration possible. When feasible, topical formulations are preferred, as for the treatment of vaginal dryness. The hormone profiles associated with choices A, B,C, D, and F are not consistent with what is typiIcally seen in women expenencing menopause.

14. The correct answer is A. The patient is a 7-year-old girl who has recently undergone a 4-cm (1.6 inch) growth spurt and has reached Tanner stage 3-sexual development. In females, Tanner stage 3 usually occurs at around 10-14 years of age.

During Tanner stage3 the breasts will begin to widen, but there is no sign of contour separation. In addition, the areola will further enlarge and become darker. Pubic hair will become darker, thicker, and cover the mons pubis.

Also important to Tanner stage 3 is the growth spurt. Most girls will experience their most rapid growth spurt during Tanner stage 3, which can coincide with idiopathic adolescent scoliosis (the condition hinted at in the patient's presentation). Axillary hair may also begin to develop during this stage.

In Tanner stage 1, the prepubertal stage, there is glandular tissue in the breasts, the areolae follow the skin contours of the chest, and there are no secondary sexual characteristics, such as pubic hair.

Tanner stage 2 is generally the onset of puberty and typically occurs in girls 8-12 years of age. The breast buds will develop and subareolar tissue will begin to elevate. Pubic hair is fine and down-like and restricted to the labia majora. Pubertal onset may be earlier in children of African descent.

Tanner stage 3 can be differentiated from earlier stages by the coarsening of pubic hair. Stage 4 can be differentiated from stage 3 by raised areola ("mound on mound "), and stage 5 by spread of pubic hair to the medial thigh.

15. The correct answer is E. It is possible to assess when ovulation has occurred by checking one's basal body temperature on a daily basis. Progesterone is produced by the corpus luteum shortily after ovulation. One of its locations of action is the hypothalamic thermoregulatory center, leading to a slightly elevated basal body temperature (up to 1°F). Normally estrogens lower core body temperature. In hypoestrogenic states such as menopause, core body temperature increases, but this effect would not be seen in a young woman Follicular stimulating hormone promotes the growth of developing follicles but does not affect body temperature. Luteinizing hormone promotes ovulation and progesterone secretion but does not affect thermoregulation. Human chorionic gonadotropin likewise does not affect body temperature, and is measurable once the woman is pregnant.

16. The correct answer is C. The 56-year-old patient presents to her primary care physician with symptoms of menopause. At menopause, estrogen production ceases

due to a decreased number of ovarian follicles. Along with low estrogen levels, postmenopausal women have high levels of luteinizing hormone (LH), follicle-stimulating hormone (FSH), and gonadotropin- releasing hormone (GnRH) due to the lack of negative feedback of estrogen on the anterior pituitary gland and hypothalamus. Because the patient is going through menopause, answer choices indicating increased estrogen (D and E) would be incorrect. The decreased amount of estrogen that would be observed in this patient would not be able to provide feedback inhibition on the other hormones. Answer choices showing a reduction in LH, FSH, or GnRH would be incorrect and do not correlate with menopause.

17. The correct answer is A. The hormone described in the question stem is glucagon. This hormone is released from pancreatic a-cells and opposes the actions of insulin. Glucagon's function is mediated through a G-protein-coupled receptor (GPCR). There is downstream activation of adenylyl cyclase and an increase in cAMPwhich serves as a second messenger that mediates subsequent physiologic actions.

Intracellular steroid receptors are mechanisms of action associated with steroid hormones. An example of a steroid hormone is cortisol.

lon channel-linked receptors cause a change in polarization across the cell membrane. Glutamate is an example of a ligand that works through an ion channel-linked receptor.

Receptor serine/threonine kinases help produce physiologic actions through phosphorylation. Transforming growth factor-beta is an example of a molecule that has its action mediated by a receptor serine/threonine kinase. Receptor tyrosine kinases phosphorylate downstream proteins and enzymes to mediate physiologic actions. This mechanism of action is associated with insulin.

18. The correct answer is E. The actions of insulin are mediated at the cellular level by binding of insulin to its receptor, followed by autophosphorylation of tyrosine residues on the insulin receptor. This generates a tyrosine kinase that participates in an intracellular signaling cascade. This is the same signaling pathway of IGF-1 (insulin growth factor 1), PDGF (platelet derived growth factor), and FGF (fibroblast growth factor). Inhibition of tyrosine kinase function would prevent downstream signaling and block the physiologic changes associated with the hormone, regardless of the amount of hormone present in the blood.

ACTH is an endocrine hormone secreted from the anterior pituitary gland that stimulates glucocorticoid steroid hormone secretion from the adrenal cortex. Upon ACTH binding to cell surface ACTH receptor, the intracellular cAMP-signaling cascade is activated to mediate secretion of glucocorticoid steroid.

BNP, or brain natriuretic peptide, is a polypeptide secreted by the ventricles of the heart to decrease systemic vascular resistance and central venous pressure, in the setting of heart failure. Upon BNP binding to its receptors (NPRA), the intracellular cGMP-signaling cascade is activated to mediate vasodilation.

Cortisol is a steroid hormone secreted from the zona fasciculata of the adrenal cortex. Upon cortisol binding to intracellular glucocorticoid receptor, it undergoes nuclear translocation to regulate gene expression.

Erythropoietin is a glycoprotein hormone that is secreted from the interstitial cells of the kidney to increase RBC production. Upon erythropoietin binding to its receptor (EpoR), intracellular non receptor tyrosine kinases transduce signals via the JAK STAT pathway.

19. The correct is C. This patient's symptoms combined with her altered facial appearance suggests a diagnosis of acromegaly, resulting from growth-hormone - secreting pituitary adenoma. Excess growth hormone leads to excess insulin-like growth factor 1 production. In adults, this can stimulate the growth of skin, connective tissue, epithelial tissues and bone, as seen in this patient. Her polyuria and polydipsia are signs of diabetes mellitus, resulting from another common metabolic derangement (reduced insulin sensitivity) that is seen with excess growth hormone. The patient's headaches may be related to the enlarged pituitary tumor.

First-line treatment for acromegaly is octreotide, a somatostatin analog. Somatostatin exerts a variety of physiologic effects throughout the body, most of them inhibitory. In the hypothalamic-pituitary axis, somatostatin and growth hormone-releasing hormone (GHRH) are released from the hypothalamus and act on the pituitary. GHRH stimulates the synthesis and release of growth hormone. Somatostatin blocks the effect of GHRH, thereby inhibiting growth hormone secretion. In the gastrointestinal system, somatostatin is released from mucosal D cells to inhibit gastric acid secretion and gastric emptying and to slow motility. In the pancreas, somatostatin reduces glucagon and insulin secretion. As a result, exogenous administration of octreotide is expected to inhibit the release of insulin. In addition, octreotide may cause nausea, vomiting, diarrhea, and gallstone-related illness. The actions and effects of somatostatin in the body are summarized in the table shown. Somatostatin may have a mild inhibitory effect on ACTH, but would not be significant in this scenario. Moreover, somastotatin does not inhibit cortisol, parathyroid hormone, or testosterone. ACTH release is stimulated by corticotropin-releasing hormone. Cortisol release is stimulated by ACTH. Parathyroid hormone is secreted in response to decreased serum Ca2 concentrations and inhibited by increased Ca levels. Testosterone release is regulated by gonadotropin-releasing hormone.

20. The correct answer is C. In a young man who is hypoglycemic and has obviously not been able to eat for a period of time, insulin secretion is decreased. Gluconeogenesis takes over as the primary source of glucose for the body. In this patient who is hypoglycemic, less glucose reaches the beta cells. As a result, less adenosine triphosphate (ATP) is made and the ATP-sensitive potassium channels remain open. The membrane fails to depolarize and calcium does not enter the cell.

Therefore, insulin granules are not released. Recall that normally with glucose intake, glucose reaches the beta cells through GLUT2 transporters, leading to production of ATP and consequent closure of ATP-sensitive potassium channels. Potassium then accumulates intracellularly leading to depolarization of the cell membrane. This depolarization activates voltage gated calcium channels which allow for entry of calcium into the cell. The increased intracellular calcium then leads to exocytosis of preformed insulin granules. In response to glucose, insulin is normally released leading to increased activation of GLUT4 transporter in adipose and striated muscle tissue. It would not be seen in hypoglycemic states. Glucose will enter beta cells, because glucose entry via GLUT2 is not an insulin-dependent process. Yet glucose entry will be limited by the low glucose circulating in the hypoglycemic state. Oxidative phosphorylation is also not inhibited, since the process is dependent on oxygen and not glucose. The limited glucose available to the body will undergo metabolism to provide energy to the body. A response to insulin binding to its receptors that caused increased expression of GLUT4 would not be seen in this case. Voltage gated calcium channels don't open since ATP-sensitive K channels are not activated in this patient. Calcium would not accumulate. Glucose still enters beta cells via GLUT2 since this process is not insulin-dependent. Oxidative metabolism depends on oxygen and is not inhibited by hypoglycemia. Beta islet cells release insulin, which is decreased in a hypoglycemic state. So beta cell islet activity would not increase. Beta cells will NOT depolarize until ATP allows for ATP-sensitive K channel activation.

Somatostatin	
Source	D cells (GI mucosa and pancreatic islets)
Action	Decrease: gastric acid, pepsinogen secretion, pancreatic ans small intestine flid secretion, gallbladder contraction and release of insulin and glucagon
Regulation	Increased by acid Decreased by vagal stimulation
Notes	Inhibitory hormone, antigrowth effects, used to treat VIPoma and carcinoid tumors

21. The correct answer is A. This patient's excessive urination (polyuria), chronic lithium use for bipolar disorder, high plasma sodium and serum osmolality levels, and inability to raise urine osmolality after water deprivation and desmopressin tests, are highly suggestive of a diagnosis of nephrogenic diabetes insipidus (0) secondary to chronic lithium use, which is a common side effect of this medication. Chronic lithium use can lead to nephrogenic DI by interfering with ADH's function of increasing water permeability at the collecting ducts. As a result of the kidney's inability to concentrate urine, free water is lost as hypotonic urine (polyuria), which leads to increased plasma sodium and osmolality. This patient's plasma osmolality is 330 mOsm/kg, so only a

urine osmolality significantly less than this value (100 mOsm/kg) would indicate hypotonic urine and diabetes insipidus. Any patient on lithium who presents with symptoms of polyuria and thirst should be evaluated for diabetes insipidus. A commonly used test is the water deprivation test, in which the patient is not allowed fluid intake while urine osmolality is measured. In patients with primary polydipsia, there will be an increase in urine osmolality because the kidneys are functioning and able to concentrate urine. Patients who fail the water deprivation test (ie, unchanged urine osmolality) are given a bolus of desmopressin. If urine
osmolality increases, a diagnosis of central diabetes insipidus (D1) is made. In central DI, ADH is not secreted from the posterior pituitary, but kidney function remains intact. In response to desmopressin, the kidneys in a patient with central Dl are able to concentrate the urine. resulting in elevated urine osmolality, If urine osmolality remains unchanged after a water deprivation test and a desmopressin challenge, then a diagnosis of nephrogenic DI is made.

The other answer options are incorrect:

An osmolality value of 290 mOsm/kg would be expected in a patient with normal functioning kidneys that respond adequately to ADH.

A urine osmolality value of 360 mOsm/kg would be expected in a patient who is dehydrated or suffering from any state in which there is an increase in water reabsorption from the kidneys.

A large increase in urine osmolality producing a value of 425 mOsm/kg can be present in patients with very severe dehydration, SIADH, glycosuria, or a high-protein diet.

A urine osmolality value of 800 mOsm/kg can be seen in a patient with primary polydipsia after undergoing a water deprivation test. The main feature in primary polydipsia is that there is stimulation of the thirst center, which causes the patient to chronically increase fluid intake.

Diagnosis of diabetes insipidus and polydipsia			
Test	Center DI	Nephrogenic DI	Primary polydipsia
Random plasma osmolarity	↑	↑	↓
Random urine osmolarity	↓	↓	↓
Urine osmolarity during water deprivation	No change	No change	↑
Urine osmolarity after IV DDAVP	↑	No change	↑
Plasma ADH	↓	Normal to ↑	↓

22. The correct is C. In the nephron, glucose is only reabsorbed from the proximal tubule. This process invo (primarily SGLT2). This transporter is located in the luminal membrane of the proximal convoluted tubule. These transporters are able to handle filtered glucose concentrations in the healthy physiologic range and above. The threshold for glucose reabsorption is reached at a glucose concentration of approximately 200 mg/dL (or a transport rate of 250 mg/min, given a glomerular filtration rate (GFRJ of 125 mL/min), Threshold occurs when some of the nephrons, but not all of them, start to reach their maximum transport level and is called "splay of the glucose titration curve." At this point glucose starts to appear in the urine

At 300 mg/dL (or a transport rate of 375 mg/min, given a GFR of 125 mL/min), however, all the transporters become saturated. This is called "transport maximum" and occurs when any further increase in glucose cannot be absorbed, and all the excess will be secreted in the urine. This difference between threshold and transport maximum occurs because some nephrons have an individual transport maximum for glucose that is lower than that of other nephrons. This introduces splay in the titration curve of transport maximum for the kidney, until all nephrons are at their maximal capacity.

Adenosine triphosphate-driven sodium-potassium exchange pumps create the sodium gradient that allows for cotransport of many molecules, including glucose. By moving sodium from the epithelial cells into the interstitial fluid/blood, the pumps create a gradient that promotes entry of sodium in the tubular lumen into the tubular epithelial cells. Although these pumps are located in all parts of the nephron, glucose resorption specifically does not take place in the distal convoluted tubule. These sodium-potassium exchange pumps also indirectly provide the energy for glucose resorption in the proximal convoluted tubule. As the sodium travels down its gradient, it passes through the sodium-glucose symporter and supplies energy for the resorption of glucose. Although an increase in serum glucose will increase the concentration of glucose filtered into tubules and transport by the sodium-glucose symporter, it should not change the function of the sodium-potassium exchange pump.

Tight junctions are not found in the glomerular capillary endothelial cells of the nephron. Tight junctions are found in the brain as a key component of the blood brain barrier of the brain and in the retinas.

23. The correct answer is A. Adipocytes are the cells that comprise adipose (fat) tissue. GLUT4 is an insulin-dependent glucose transporter and it is found in only two tissue types: adipose tissue and skeletal muscle. In the fasting state, when insulin levels are low, there is decreased intake of glucose into adipose tissue and skeletal muscle, enabling glucose to be utilized by more pertinent organs. In this context, decreased glucose intake into fat and muscle cells will promote mobilization of stored precursors such as amino acids and free fatty acids. This is the only choice among those listed that could be used in the hypothetical experimental system described.

24. The correct answer is A. The steroid hormone circulates in the plasma bound to a hormone-specific binding globulin. At the target organ, it crosses the cell membrane due to its lipophilic properties and binds to an intracellular receptor either in the cytoplasm or within the nucleus. The hormone-receptor complex then undergoes a conformational change, which reveals the receptor's DNA-binding domain; without this step, it is unable to carry out its action and bind to DNA. Once the binding domain is revealed, the hormone-receptor complex binds the DNA enhancer element and causes changes to gene expression at the transcriptional level. Binding of the steroid hormone to a hormone-specific globulin helps the hormone reach its target cell population, but does not immediately precede binding to DNA. Steroid hormones do not act through transmembrane receptors and second messengers. Although binding to a DNA enhancer element is the desired action of the hormone, this is the final step in its signaling pathway, not the one immediately preceding it. Binding to an intracellular steroid receptor alone is also not the correct answer, since conformational change of the hormone-receptor complex must occur before the steroid hormone-receptor complex binds to DNA.

25. The correct answer is E. This patient is a 6-year-old otherwise healthy girl who is presenting with accelerated growth, thelarche, and adrenarche consistent with central precocious puberty. A patient should be evaluated for precocious puberty when the onset of secondary sexual characteristics occurs before 8 years of age for girls and 9 years of age for boys.

There are two main types of precocious puberty: central and peripheral. Central precocious puberty is known as gonadotropin-dependent precocious puberty. The symptoms of central precocious puberty mimic the stages of normal puberty: girls present with sequential development of breasts and pubic hair, and boys present with sequential development of the penis and testes followed by pubic hair. Central precocious puberty is either idiopathic or caused by a central nervous system (CNS) lesion. Idiopathic precocious puberty is caused by premature maturation of the hypothalamic-pituitary-gonadal (HPG) axis and associated pulsatile gonadotropin releasing hormone (GnRH) release from the hypothalamus. Pulsatile GnRH secretion stimulates FSH and LH release from the pituitary gonadotropic cells. Eighty to 90 percent of cases of central precocious puberty in females are idiopathic in nature. In contrast, central precocious puberty is commonly pathological in boys, with 40-759% of cases having a pathological cause. CNS lesions are the most likely pathological causes of central precocious puberty, and thus all patients presenting with precocious puberty-even females - should be evaluated with cranial MRI.

Peripheral precocious puberty is caused by excess sex hormone secretion (estrogens and/or androgens) from either the gonads or adrenal glands (or exogenous sources).

High levels of sex hormones exert negative feedback on the release of GnRH, follicle-stimulating hormone (FSH) and luteinizing hormone (LH). Thus, FSH and LH levels are suppressed (in the prepubertal range) and do not increase substantially with gonadotropin-releasing hormone (GnRH) stimulation. There are various causes of peripheral precocious puberty, including ovarian tumors and ovarian cysts in girls and testicular tumors (leydig cell) and hCG-secreting germ cell tumors in boys. Both boys and girls can develop peripheral precocious puberty from primany hypothyroidism, McCune-Albright syndrome, adrenal pathology, or endogenous sex steroid administration.

The incorrect answers are not the best choices.

Continuous stimulation of the pituitary gonadotropic cells by gonadotropin releasing hormone (GnRH) would in fact lead to decreased pubertal development due to suppression of FSH/LH release from pituitary gonadotropic cells because secretion of FSH and LH occurs only in response to pulsatile GnRH secretion. Clinicians who are aiming to delay pubertal development in their patients with central precocious puberty often prescribe continuous GnRH.

Non-classic 21-hydroxylase deficiency can present at an older age compared to classic 21-hydroxylase deficiency because patients retain some 21-hydroxylase functioning as part of this condition. However, in females, this disorder would present similar to polycystic ovarian syndrome, with oligo/amenorhea, hirsutism and clitoral enlargement, none of which this patient is experiencing.

McCune-Albright syndrome (MAS) is caused by a somatic (postzygotic) mutation of the alpha subunit of the Gs protein that activates adenylyl cyclase, leading to continued Gs protein activity in the absence of peripheral stimulation. Patients can present with various combinations of endocrine syndromes (peripheral precocious puberty, thyrotoxicosis, gigantism or acromegaly, Cushing syndrome, etc). Patients also classically present with fibrous dysplasia of bone and cafe-au-lait spots.

In females, germinoma presents as a primary brain tumor in the pineal gland and suprasellar region. Like other CNS lesions, germinomas can cause precocious puberty. However, in females-particularly patients Iike this who present without any neurological signs or vision abnormalities (ie, Parinaud syndrome)-idiopathic precocious puberty is a much more likely cause. This patient should have MRI to rule out germinoma as a possible cause.

26. The correct answer is B. A patient with Tanner stage IlI breast development, menarche, and pubic hair at 8 years old is should be evaluated for precocious puberty. When precocious puberty is suspected, the initial work up involves radiography of the hands and wrists to determine the bone age. This helps determine if precocious puberty is actually present and, if so, its speed of progression. If the radiograph demonstrates bone age that is within 1 year of the chronological age, puberty has not started, or the

pubertal process has been relatively brief. If the radiograph shows bone age that is 2 years or more from the chronological age, puberty has been present for a year or more, or is progressing rapidly. If the bone age test is positive, the next step in work-up involves the GnRH stimulation test. This test is used to differentiate between central and peripheral precocious puberty, and is considered the gold standard to identify central precocious puberty. Patients are administered GnRH, then LH and FSH levels are measured about 120 minutes after. If FSH levels are much greater than LH levels, this is a normal prepubertal response. In central precocious puberty, LH will be increased. If both LH and FSH are suppressed and accompanied by increased levels of testosterone or estradiol, this suggests peripheral precocious puberty, or precocious pseudopuberty. If there is no increase in LH and FSH, this is diagnostic for peripheral precocious puberty. If the GnRH test is suggestive of central precocious puberty, an MRI can be obtained to determine if there is a CNS disease, such as a tumor or hamartoma. Some central etiologies include gonadotropin-producing tumors of the hypothalamus or pituitary gland. Peripheral etiologies include gonadal tumors, adrenal tumors, and germ cell tumors. Congenital adrenal hyperplasia is a possible differential to consider, and can be confirmed by obtaining 17-0H progesterone levels, however, a bone age test should be performed first to confirm there is indeed precocious puberty.
The other answer options are not the most appropriate next step in this patient's case. Obtain an MRI if central precocious puberty is suspected following the GnRH stimulation test, but not before. The GnRH stimulation test is the next step in workup if the bone age test is positive and shows precocious puberty, but bone age test would be done first. A hormonal analysis helps determine the cause if peripheral precocious puberty is suspected, but a bone age test is done first. Reassurance is not appropriate in this case. This patient should have some work-up done as she is presenting with pubertal symptoms at age 8 which would be considered pre-pubertal. A pelvic ultrasound should be obtained if peripheral precocious puberty is suspected, but it is not the next step in this patient's case.

CLINICAL CASES

1. A previously healthy 30-year-old woman visits her physician complaining of a racing heart, sweating, weight loss, and tremulousness. She appears anxious, and on further questioning reports that her anxiety and restlessness have begun to cause problems at her workplace. Physical examination reveals tachycardia, moist skin, fine body hair, and bilateral bulging of her eyes.

1.1 What is the most likely diagnosis?

Graves disease.

1.2 What demographic group does this condition typically affect?

Graves disease occurs eight times more frequently in women than men. the prevalence is higher in populations with a high iodine intake. the disease rarely occurs before adolescence and typically affects individuals in the fourth to sixth decades of life.

1.3 What is the pathophysiology of this condition?

It is caused by autoimmune-induced hyperthyroidism. Immunoglobulins mimic thyroid-stimulating hormone (tSh) and activate the tSh receptor.

1.4 What are other common causes of hyperthyroidism?

Iatrogenic: excess thyroid hormone medication. • Silent thyroiditis: Inflammation of the thyroid gland, which progresses from hyperthyroidism to hypothyroidism.

Struma ovarii: Ovarian neoplasm (mature teratoma) that contains thyroid tissue.

Subacute thyroiditis: Inflammation of the thyroid gland thought to be secondary to viral infection.

Thyroid adenoma: Benign thyroid neoplasm.

Toxic multinodular goiter (Plummer disease): enlarged thyroid gland containing multiple active nodules that produce thyroid hormone (called “hot” nodules because of their active appearance on radioactive iodine scans.) Note: Infiltrative ophthalmopathy and pretibial myxedema is seen only in hyperthyroidism caused by Graves disease.

1.5 What are the appropriate treatments for this condition?

Graves disease can remit and recur. effective treatment includes thyroidectomy, thyroid-inhibiting medications, or radioactive iodine ablation (radioactive iodine is taken up by, and then destroys, hyperfunctioning thyroid tissue). Medications such as propylthiouracil (ptU) and methimazole inhibit iodine organification and coupling in the thyroid. ptU and steroids also inhibit the peripheral conversion of thyroxine to triiodothyronine.

1.6 What is thyroid storm?

Thyroid storm is an acute, life-threatening surge of thyroid hormone in the blood, usually precipitated by surgery, trauma, infection, acute iodine load, or long-standing hyperthyroidism. Manifestations include tachycardia (> 140/min), heart failure, fever, agitation, delirium, psychosis, stupor, and/or coma. Gastrointestinal symptoms can also

be present. this condition is treated with methimazole and agents that reduce peripheral conversion of T4 to triiodothyronine.

2. A 62-year-old woman presents to her physician with a month-long history of vague abdominal pain, constipation, and nausea and vomiting. She also has experienced diffuse bone pain over the past month, which she attributed to "just getting old." Physical examination reveals diffuse abdominal tenderness. Relevant laboratory findings are as follows: Sodium: 140 mEq/L Calcium: 12.3 mg/dL Chloride: 110 mEq/L Bicarbonate: 26 mEq/L Potassium: 4.0 mEq/L Phosphate: 2.0 mg/dL Blood urea nitrogen/creatine: 20:1.2 mg/dL

2.1 What is the most striking laboratory finding?

Hypercalcemia. Common causes of hypercalcemia are: malignancy, Intoxication with vitamin D, Sarcoidosis, Hyperparathyroidism, Alkali syndrome, and Paget disease of bone (mnemonic: mISHAP). In outpatients, hyperparathyroidism is the most common cause of hypercalcemia; in inpatients, malignancy is the most common cause.

2.2 How is calcium regulated in the body?

Parathyroid hormone (PTH) stimulates osteoclasts to resorb calcium from bone; increases calcium reabsorption in the distal convoluted tubules of the kidney; increases production of 1,25-(Oh)2 vitamin D by the kidney; and decreases renal reabsorption of phosphate.

Vitamin d promotes calcium reabsorption from bone and the small intestine.

Calcitonin inhibits osteoclast activity, thereby decreasing reabsorption of calcium from bone. In normal calcium homeostasis, calcitonin is likely not as significant.

2.3 The patient is found to have elevated PTH and normal creatine. How does this help explain her clinical presentation?

The patient has primary hyperparathyroidism, as evidenced by high pth, high calcium, and normal renal function. to recall the symptoms of hyperparathyroidism (and hypercalcemia in general) use the following mnemonic: "painful bones, renal stones (nephrolithiasis), abdominal groans (abdominal pain, nausea, vomiting, and anorexia), psychic moans (changes in mental status, concentration, and mood), and fatigue overtones."

2.4 What is the appropriate treatment for acute, severe forms of this condition?

Hydration. If the electrolyte abnormality persists, a loop diuretic can be used (to increase calcium excretion). If needed, calcitonin and bisphosphonates can also be prescribed.

2.5 What is the most appropriate long-term treatment for this patient?

Parathyroidectomy. Surgery for primary hyperparathyroidism has cure rates of 96%–98%.

3. A 52-year-old woman presents to the clinic with several months' history of generalized weakness, cold intolerance, and weight gain. Physical examination reveals

alopecia, a thick and beefy tongue, myxedema, and delayed deep tendon reflexes. Her heart rate is 55/min and her blood pressure is 100/70 mm Hg. She is not taking any medications. Relevant laboratory findings are as follows: Free thyroxine (T4): 4.5 pmol/L (normal: 10.3–35 pmol/L) Thyroid-stimulating hormone (TSH): 31 μU/mL (normal: 0.8–2 μU/mL) Cholesterol: 230 mg/dL

3.1 What is the most likely diagnosis?

The patient's cold intolerance, weight gain, myxedema, fatigue, prolonged relaxation phase of deep tendon reflexes, and low free T4 with high tSh suggest primary hypothyroidism.

3.2 What is the most common cause of this condition?

Hashimoto thyroiditis (autoimmune destruction of the thyroid gland). patients are typically positive for antithyroid peroxidase (antimicrosomal) antibodies. additional causes of hypothyroidism include riedel thyroiditis, subacute thyroiditis, and silent thyroiditis. the prevalence of hashimoto thyroiditis is increased in patients with other autoimmune disease such as vitiligo.

3.3 What endocrine disorder is associated with low free T4 and low serum TSH levels?

Low T4 levels in the setting of low or normal tSh levels imply secondary hypothyroidism, the most common cause of which is hypopituitarism. Other manifestations of hypopituitarism include sexual dysfunction and diabetes insipidus.

3.4 What is the appropriate treatment for this condition?

Levothyroxine (synthetic T4 hormone). Levels of T4 typically take 4–6 weeks to reach steady state after initiation of therapy.

3.5 How are thyroid hormones produced and metabolized?

Iodine is essential for the production of thyroid hormones in the follicular cells of the thyroid gland. Following T4 production in the thyroid gland, deiodinases in the peripheral tissues convert T4 to the active form, T3.

3.6 What are the primary functions of thyroid hormones in the peripheral bloodstream?

T3 has a role in brain maturation, bone growth, β-adrenergic effects, and increasing the basal metabolic rate.

4. A 77-year-old man is brought to the clinic by a concerned neighbor to evaluate a large neck mass. According to the neighbor, the patient lives alone and keeps to himself. The neighbor has noticed that the neck mass has enlarged over several months. meanwhile, the patient has lost approximately 5.4 kg (12 lb) and has developed noticeable tremor when he reaches for his morning paper or walks his dog. on physical examination, the man is thin with a large goiter containing many palpable nodules. ECG reveals atrial fibrillation. Exophthalmos and pretibial myxedema are absent.

Thyroid function tests reveal elevated free thyroxine (T4) and barely detectable thyroid-stimulating hormone levels.

4.1 What is the most likely diagnosis?

Plummer disease (also known as toxic multinodular goiter) is the second most common cause of hyperthyroidism in the Western world after Graves disease and the number one cause among the elderly and in endemic areas of iodine deficiency. this is not to be confused with the uncommon Plummer-Vinson syndrome (esophageal web plus iron deficiency anemia).

4.2 How does the physical examination help establish a differential diagnosis?

Patients with Graves disease typically have a diffusely enlarged painless goiter rather than a multinodular goiter. exophthalmos, pretibial myxedema, and acropachy (thickening of peripheral tissues), characteristic of Graves disease, are absent in plummer disease. Subacute thyroiditis (also known as de Quervain thyroiditis) presents with an enlarged painful goiter (Figure 6-13), neck pain, and fever, frequently after a viral illness such as mumps or coxsackievirus. the erythrocyte sedimentation rate is typically elevated, and the condition resolves with time and use of nonsteroidal anti-inflammatory drugs.

4.3 What are the signs and symptoms of local compression by a neck mass?

Symptoms: dysphagia (difficulty swallowing), dysphonia (hoarseness), and dyspnea (difficulty breathing). Signs: stridor, tracheal deviation, superior vena cava syndrome. (pemberton sign is engorgement of the facial and neck veins upon simultaneous raising of the arms overhead, secondary to superior vena cava compression at the thoracic inlet.)

4.4 What will a radioactive iodine scan likely show?

A thyroid scan with radioactive iodine or tc99m will likely show patchy uptake, with multiple “hot” nodules interspersed among areas with decreased uptake. a “hot” nodule means that the activity of the thyroid tissue in that area is elevated. patients with Graves disease have homogenously high uptake on thyroid scan, whereas patients with thyroiditis (de Quervain or silent lymphocytic thyroiditis) have low uptake on thyroid scan. In general, nodules containing thyroid cancer tend to be “cold” nodules and should be biopsied via fine-needle aspiration.

4.5 What is the appropriate treatment for this condition?

Given the size of his goiter, signs of local compression, and symptoms of hyperthyroidism, thyroidectomy should be performed. this will alleviate the symptoms of hyperthyroidism in approximately 90% of cases and will rapidly relieve the compression. preoperatively, the patient should be treated with antithyroid medication (such as methimazole) and β-blockers to render him euthyroid and to alleviate the atrial fibrillation.

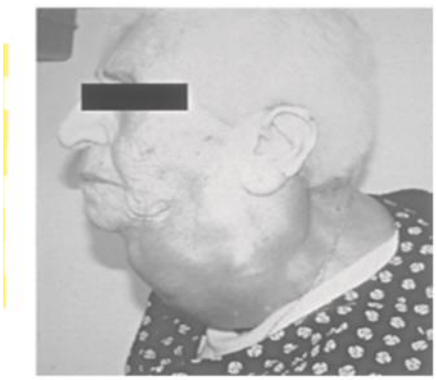

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FIGURE 6-13 A large multinodular goiter.

5. A 23 year old woman is admitted to the hospital with the chief complaint of 2 weeks of neck swelling. A farmer and mother of 2 children, she delivered her last child 3 months ago after a normal term pregnancy, and resumed working in the fields 2 months ago. She was in her usual state of fully functional health until two weeks ago when she noticed a painless swelling in the lower part of her neck associated with sweats and feeling "hot" all the time. She went to a clinic and received medications for malaria which didn't help. The swelling has progressively increased and she now feels uncomfortable when swallowing. Her heart is "pumping fast", she tires easily while working, and she hasn't been sleeping well; She's noted no change in weight but an increased appetite.

What is most likely diagnosis.

6. A 28 year old woman presents to the hospital complaining of 4 months of "heart pains". The pains started about 4 months ago, felt initially on climbing hills, and described (with her hand fluttering in the air) as her heart pounding very fast on mild exertion. The problem has progressed: now she's experiencing the "pain" for hours even at rest - a rapid fluttering and vague discomfort in her chest. In addition, she always feels "hot", even in the rainy season, is more comfortable at night than during the day, and always feels hungry - eating more than usual and gaining weight. She's noted no change in her bowel or sleep habits, or mood. She's had no joint pains, fevers, changes in her vision or eyes, but complains of her hair falling out. Upon direct questioning, she notes that there's been an increased fullness in her lower neck region but is unsure of its duration.

"I've just not been feeling right doctor, I feel terrible in fact. I'm losing weight, my bowels have taken a turn for the worse and I'm struggling to sleep. I'm really worried, my heart is racing sometimes, I think something is seriously wrong." I've lost about 8kg over the last 6 months. My appetite has been fine, I've been eating more if anything! I go to the gym twice and week and have done for many years, so no change there. "The heart racing really scares me, I keep worrying I'm having a heart attack. It seems to come on suddenly at random intervals, I can't identify any triggers. I don't get any chest pain or shortness of breath, but I sometimes feels a bit dizzy. I haven't

ever lost consciousness though. It's hard to say if it's regular, I'm pretty sure it's irregular to be honest, but I couldn't be totally sure."Sorry I forgot to mention that I've also been feeling a bit shaky, my hands at times really tremble, despite me not being particularly anxious, it's really weird. Her hands are warm and sweaty.
What is most likely diagnosis.

7. A 30-year-old female demonstrated a subtle onset of the following symptoms: dull facial expression; droopy eyelids; fast fatigue; dry hair; dry, scaly skin; evidence of intellectual impairment;; bradycardia (60 b/min); a blood pressure of 90/70; constipation, and hypothermia. Plasma concentrations of elevated TSH levels.
What is most likely diagnosis.

8. Josie owns a business, has several employees, and works hard to manage her business and make time for her family. Over several months, she slowly recognized that she felt warm when others did not; she sweated excessively and her skin was often flushed. She often felt as if her heart were pounding, she was much more nervous than usual, and it was diffi cult for her to concentrate. She began to feel weak and lose weight, even though her appetite was greater than normal. Her family recognized some of these changes and that her eyes seemed larger than usual. They encouraged her to see her physician. Based on the symptoms, her physician suspected that Josie was suffering from hyperthyroidism. A blood sample was taken and the results indicated that her blood levels of thyroid hormones were elevated and her blood levels of TRH and TSH were very low. In addition, a specific immunoglobulin, called thyroid-stimulating immunoglobulin (TSI), was present in significant concentrations in her blood. The structure of TSI is very similar to the structure of TSH. The physician concluded that Josie was suffering from Graves disease. Josie was treated with radioactive iodine (131I) atoms, which were actively transported into Josie's thyroid cells, where they destroyed a substantial portion of the thyroid gland. Subsequently, Josie had to take thyroid hormones in the form of a pill to keep her blood levels of thyroid hormones within their normal range of values.
Predict

a. Prior to treatment, explain why Josie's blood levels of thyroid hormones were elevated.

b. Prior to treatment, why were her TRH and TSH levels lower than normal?

c. After the 131I treatment, why are her thyroid hormone levels lower than normal?

d. After the 131I treatment, predict what will happen to Josie's TRH and TSH levels.

e. Why will Josie have to take thyroid hormone pills for the rest of her life? What effect will that have on her TRH and TSH levels

9. A 50-year-old male had a total thyroidectomy followed by thyroid hormone-replacement therapy. Thirty-six hours later he developed laryngeal spasms, a mild tetany, and cramps in the muscles of the hands and arms. What is most likely diagnosis.

10. Suppose that a person has a pituitary gland tumor that causes an overproduction of TSH. Would the blood levels of TRH and thyroid hormones be normal, higher than normal, or lower than normal? Explain.

11. A 4-year-old girl with a history of ambiguous genitalia is brought to her pediatrician for a check-up. The child's blood pressure is found to be 130/89 mm Hg. Physical examination is notable for clitoral enlargement, partial labial fusion, and scant pubic hair growth. Laboratory tests reveal the following: Sodium: 142 mEq/L Potassium: 3.1 mEq/L Chloride: 102 mEq/L Bicarbonate: 25 mEq/L

11.1 What enzyme-deficiency is this?

11β-Hydroxylase deficiency is suggested by the constellation of hypertension, masculinization, and hypokalemia.

11.2 How is this condition differentiated from a more common, but similar, enzyme deficiency?

21β-Hydroxylase deficiency presents with hypotension and hyperkalemia. Both deficiencies present with masculinization of the external genitalia

11.3 How does this enzyme deficiency result in hypertension?

11β-hydroxylase converts 11-deoxycorticosterone into corticosterone, and 11-deoxycortisol into cortisol. 11β-hydroxylase deficiency causes a lack of cortisol and aldosterone. however, the precursor 11-deoxycortisone is a weak mineralocorticoid and causes hypertension.

11.4 What is the appropriate treatment for this condition?

Dexamethasone or hydrocortisone can be used to replace the missing corticosteroid. the lowest effective dose should be used to avoid the Cushingoid adverse effects of glucocorticoids, including bone demineralization and growth retardation.

11.5 What is the mode of inheritance of this condition?

Inheritance is autosomal recessive, with mutations in the CYP11B1 gene. all of the congenital adrenal hyperplasias are inherited in an autosomal recessive manner

12. A 40-year-old woman visits her physician because of fatigue and weakness, which she has experienced for several months. She says she often feels lightheaded when she first gets out of bed in the morning or stands suddenly. Review of symptoms is positive for frequent headaches, nausea, and vomiting. Her vital signs are notable for a blood pressure of 125/75 mm Hg seated and 105/60 mm Hg standing. Physical examination reveals several patches of hyperpigmentation on the skin. Relevant laboratory findings are as follows: Sodium: 126 mEq/L Bicarbonate: 19 mEq/L Potassium: 5.2 mEq/L Cortisol: 4.3 mg/dL Chloride: 97 mEq/L

12.1 What is the most likely diagnosis?

Addison disease, or primary adrenal insufficiency, is suggested by the clinical history of weakness and orthostatic hypotension and by the signs of hyperpigmentation, hyponatremia, hyperkalemia, and a low serum cortisol level.

12.2 What are common etiologies of this disease?

Most cases of Addison disease are idiopathic or autoimmune related. Other causes include the following: • Disseminated intravascular coagulation. • Waterhouse-Friderichsen syndrome (hemorrhagic necrosis of the adrenal gland, classically due to meningococcemia). • Granulomatous diseases such as tuberculosis. • HIV infection. • Neoplasm. • trauma. • Iatrogenic vascular disorders.

12.3 What is the cause of this patient's metabolic abnormalities?

Adrenal insufficiency causes a deficiency of cortisol. hyponatremia, hyperkalemia, and a low bicarbonate level can result from low aldosterone levels associated with primary adrenal insufficiency.

12.4 How would this patient's cortisol level change if she were administered adrenocorticotropic hormone (ACTH)?

The cortisol level should not change appreciably since it is low because of a primary adrenal insufficiency (ie, the problem is within the adrenal gland itself). this is suggested by the hyperpigmentation, which is due to the attempt of the pituitary gland to overcome the cortisol deficiency by increasing ACTH production. ACTH, in turn, stimulates the release of melanocyte-stimulating hormone, causing hyperpigmentation.

12.5 What are the secondary and tertiary forms of this condition?

Secondary adrenal insufficiency is caused by decreased ACTH secretion by the pituitary gland. administration of ACTH results in a cortisol response. this syndrome does not cause hyperpigmentation. Tertiary adrenal insufficiency is caused by a decrease in corticotropin-releasing hormone production by the hypothalamus.

13. A 35-year-old woman presents to her internist complaining of recent episodes of weakness and tingling in her extremities. She also complains of polyuria, nocturia, and polydipsia. Although her blood pressure has been normal in the past, on the day of this visit it is 160/100 mm Hg. Laboratory studies reveal a serum sodium level of 147 mEq/L, a potassium level of 2.8 mEq/L, and very low serum renin activity.

13.1 What is the most likely diagnosis?

Primary hyperaldosteronism, also known as Conn syndrome, is suggested by the patient's history and her hypertension, hypernatremia, and hypokalemia. approximately 30%–60% of cases are due to solitary adrenal adenomas in the zona glomerulosa, the aldosterone-secreting layer of the adrenal cortex. Bilateral hyperplasia of the zona glomerulosa can also cause Conn syndrome.

13.2 How is aldosterone regulated?

Renin, produced by the juxtaglomerular cells of the kidney, cleaves angiotensinogen (produced by the liver) to form angiotensin I. angiotensin I, in turn, is cleaved by angiotensin-converting enzyme to form angiotensin II. In response to volume contraction, angiotensin II becomes a potent stimulator of aldosterone synthase, a key

enzyme in aldosterone synthesis. Other key stimuli of aldosterone secretion include decreased plasma sodium and increased plasma potassium.

13.3 Another patient presents with similar symptoms, but his laboratory tests show increased serum renin activity. What is his most likely diagnosis?

Hypertension has a variety of causes. approximately 95% of patients with hypertension have primary or "essential" hypertension, which has no identifiable cause. the remaining patients have secondary hypertension, which is caused by an identifiable underlying etiology such as extra-adrenal hyperstimulation of aldosterone secretion.

	Primary hypertension	Secondary hypertension
Cause	Genetic factors, including conditions such as Bartter syndrome and Gitelman syndrome.	• Vascular disease/renal hypoperfusion (renal artery stenosis, decreased effective circulating volume). Endocrine disorders (renin-secreting tumors, Conn syndrome, Cushing syndrome, pheochromocytoma). Intrinsic renal disease (chronic renal failure, glomerulonephritis).
Labs	Decreased renin levels.	Increased renin levels.

13.4 What is the appropriate treatment for this condition, and what are the adverse effects?

If a solitary, aldosterone-secreting adrenal adenoma is found, surgical resection (adrenalectomy) is indicated. Bilateral adrenal hyperplasia is treated medically with an aldosterone antagonist such as spironolactone. Major adverse effects of spironolactone are due to its antiandrogen effects, including gynecomastia, loss of libido, menstrual irregularities, and impotence.

14. A 36-year-old woman with no significant medical history presents to her primary care physician with a 6-month history of amenorrhea, weight gain, and excessive facial hair growth. She denies any recent diet or medication changes. Her vital signs are notable for a pulse of 80/min and blood pressure of 148/90 mm Hg. Physical examination reveals a well-developed hirsute female with truncal obesity, abdominal striae, and peripheral edema. She has difficulty arising from a chair during her neurological exam. Relevant laboratory findings are as follows: Sodium: 140 mEq/L Bicarbonate: 25 mEq/L Potassium: 3.4 mEq/L Chloride: 92 mEq/L Glucose: 225 mg/dL

14.1 What is the most likely diagnosis?

Cushing syndrome results from excess glucocorticoids, either from increased cortisol production or exogenous glucocorticoid therapy. Common causes include the following: iatrogenic (eg, steroid ingestion, most common); pituitary adenoma (Cushing disease); adrenal tumor/hyperplasia; adrenocorticotropic hormone (ACTH)-producing tumor (most commonly secondary to small cell lung cancer).

14.2 What laboratory tests can help confirm the diagnosis?

Screening tools for Cushing syndrome or glucocorticoid excess include the following: 24-hour urine free cortisol test. elevated cortisol level indicates hypercortisolism. Dexamethasone suppression test. A normal result is a decrease in cortisol after administration of lowdose dexamethasone. In glucocorticoid excess due to Cushing disease, low-dose dexamethasone will not suppress cortisol levels.

14.3 After identifying elevated cortisol levels, what diagnostic tests help define the source of the hormonal abnormality?

Serum ACTH levels: high ACTH: pituitary adenoma or an ectopic ACTH-producing neoplasm. Low ACTH: adrenal tumor/hyperplasia or exogenous glucocorticoid administration. A high-dose dexamethasone suppression test can differentiate between a pituitary adenoma and an ectopic ACTH-producing tumor. pituitary adenomas are suppressed by high-dose ACTH, whereas ectopic ACTH-producing tumors usually are not.

14.5 What are the appropriate treatments for this condition? the most appropriate treatment for adrenal tumors is surgery.

Treatments for nonresectable tumors or hyperplasia are as follows: Ketoconazole: inhibits glucocorticoid production. Metyrapone: inhibits cortisol formation in adrenal pathway. Aminoglutethimide: inhibits the synthesis of steroids.

14.6 What is the regular cycle of cortisol levels in the body?

Cortisol levels peak in the early morning (approximately 8 am) and reach their lowest levels at midnight. Basal body temperature fluctuates with the cortisol cycle (Figure 6-3).

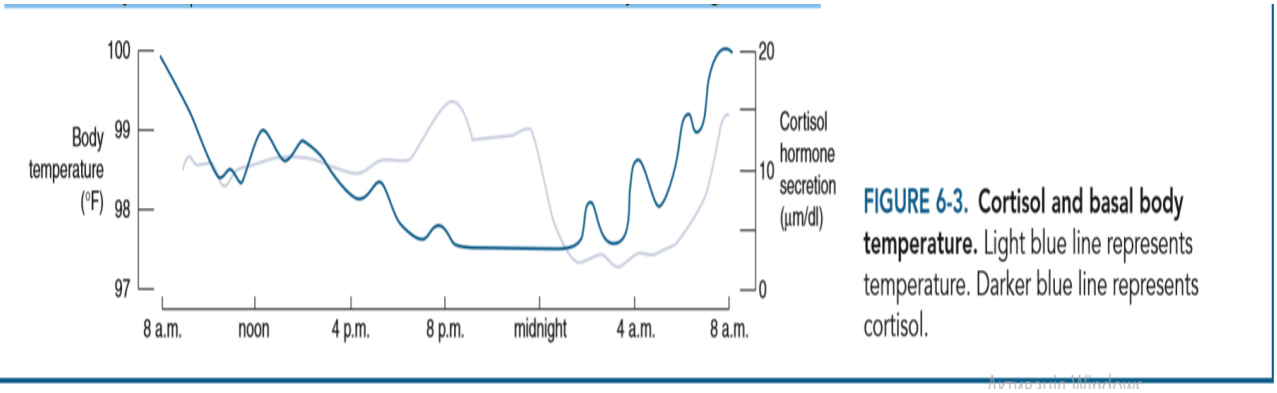

FIGURE 6-3. Cortisol and basal body temperature. Light blue line represents temperature. Darker blue line represents cortisol.

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15. A 50-year-old woman presents to the emergency department complaining of 2 hours of vertigo, headache, palpitations, blurry vision, and diaphoresis. She has a history of occasional tension headaches but no significant cardiac history. She does not smoke and has no history of hypertension. At presentation her blood pressure is 200/140 mm Hg, her heart rate is 120/min, and she is afebrile. Her skin is sweaty and flushed. noncontrast imaging of the brain is negative for blood or other mass lesions. Her blood pressure is stabilized pharmacologically. Laboratory testing reveals increased plasma metanephrine and normetanephrine levels. Results of a serum thyroid-stimulating hormone test are within normal limits. Twenty-four-hour urine catecholamines and meta/normetanephrines are elevated.

15.1 What is the most likely diagnosis?

Pheochromocytoma is a catecholamine-secreting tumor of chromaffin cells of the adrenal medulla.

15.2 What are the key steps in epinephrine catabolism?

Catecholamines are substrates for monoamine oxidase (MaO) and catechol-O-methyltransferase (COMt). Epinephrine can undergo two paths of catabolism. In the first, COMt converts epinephrine into metanephrine, which MaO then converts into 3-methoxy-4hydroxymandelic acid. In the second, MaO converts epinephrine into dihydroxymandelic acid, which COMt then converts into 3-methoxy-4hydroxymandelic acid (the same product as the first pathway).

15.3 What receptors do catecholamines act on to produce hypertension?

Catecholamines act on α1 and β1 receptors. activation of α1 receptors contracts vascular smooth muscle, and activation of β1 receptors in the heart increases heart rate, conduction velocity, and contractility.

15.4 During removal of an adrenal gland, the surgeon must secure the adrenal vasculature, especially the adrenal vein. How is the blood supplied to the adrenal gland?

The arterial blood supply to the adrenal gland can be variable, with blood supply from the superior suprarenal artery originating from the inferior phrenic artery; the middle suprarenal artery originating from the aorta; and the inferior suprarenal artery originating from the renal artery. the adrenal gland typically has a dominant vein, which empties into the left renal vein (left adrenal gland) and the inferior vena cava (right adrenal gland).

15.5 What is the probability that this patient's condition is malignant?

Approximately 10%. remember the "rule of 10's" for pheochromocytomas: 10% are malignant, 10% bilateral, 10% extra-adrenal, 10% calcify, 10% are pediatric, 10% are familial, and they are 10 times more likely to appear on the boards than in real life!

15.6 What is the structure and function of the adrenal gland?

The adrenal gland is composed of the cortex and medulla, each with its own secretory products. the zones of the adrenal cortex can be remembered with the memory trick, “the deeper you go, the sweeter it gets”: salt-related hormones (aldosterone) from the zona glomerulosa, sugar-related hormones (cortisol) from the zona fasciculata, and sex-related hormones (testosterone, DheaS) in the zona reticularis. the adrenal medulla produces catecholamines such as epinephrine and norepinephrine.

16. 25-year-old gentleman was presented to the endocrine clinic in November 2013 with a history of tiredness, reduced libido and inability to father a child for more than a year. He had a child with a previous partner, and his current female partner had already been fully evaluated by the fertility specialist. In 2007, he took anabolic steroids during body-building training, but stated that he had symptoms of tiredness and reduced libido before then. In 2011, he stopped taking the steroids because he wanted to father a child with his partner. After a year of no success, he and his partner decided to seek fertility treatment. On examination, he was well with normal secondary sexual features and normal looking external genitalia . What hormonal dysfunction could you predict.

17. A 17-year-old girl presents to the clinic for primary amenorrhea. She reports that she has never had a period. Physical examination reveals normally developed breasts, the lack of axillary and pubic hair, and a small right inguinal mass.

17.1 What is the most likely diagnosis?

Androgen insensitivity syndrome (also known as testicular feminization syndrome) should be suspected in a woman with primary amenorrhea, little or no axillary/pubic hair, and an inguinal mass. the disease affects approximately 1:100,000 chromosomal males.

17.2 What is the clinical presentation of this condition?

There are two main presentations of this disorder: • In newborns it presents as an inguinal mass. • In adolescents it presents as primary amenorrhea. the inguinal mass seen in newborns is caused by aberrant descent of the testes, which usually remain in the abdomen.

17.3 What is the pathophysiology of this condition?

This disorder results from dysfunction of the androgen receptors in a genetically male patient. the testes are present and secrete testosterone and müllerian inhibiting factor (MIF). however, the person cannot respond to this testosterone because the peripheral receptors are nonfunctional. Instead, the testosterone is converted into estradiol in peripheral tissues (especially adipose tissue), which initiates breast development. the vagina is often present but may be short and blind-ending. the MIF secretion inhibits normal development of the ovaries and uterus. Figure 13-2 illustrates genetic regulation of gonadal development.

17.4 What would confirmatory testing show in this condition?

On karyotype, these patients are 46,XY. Pelvic ultrasound can show testes and the absence of a uterus and ovaries. Polymerase chain reaction assay can show mutations of the androgen receptor. Testosterone and dihydrotestosterone (Dht) levels should also be measured. Both should be normal or high. Low testosterone may indicate testicular dysgenesis or Leydig cell aplasia/hypoplasia. If testosterone levels are normal but Dht levels are low, 5α-reductase deficiency is suspected because testosterone is converted to Dht by 5α-reductase.

17.5 What is the appropriate treatment for this condition?

Initially, removal of the testes is performed because of the high risk of cancer development without such a procedure. thereafter, treatments are mainly hormone replacement therapy and psychological support. estrogen, but not progesterone, is given because no uterus is present. estrogen is given to replace the loss of sex hormone production with the removal of the testes. psychological therapy is given because of the potential for gender confusion. Surgical reconstruction may be needed to create a "functional" vagina, although if found earlier the use of dilators may obviate surgical intervention.

18. A mother brings her 7-year-old son in to see the pediatrician. She says the boy has been less active and has also begun wetting his bed again, something he had stopped doing 2 years ago. Chart review reveals that within the past year the child's weight dropped from the 75th percentile to the 50th percentile even though he has been eating and drinking more than usual, the mother reports. Relevant laboratory findings include the following: WBC count: 11,400/mm3, normal differential Chloride: 100 mEq/L Blood urea nitrogen: 14 mg/dL Sodium: 132 mEq/L Creatinine: 1.2 mg/dL Potassium: 5.0 mEq/L Glucose: 350 mg/dL

18.1 What is the most likely diagnosis?

Autoimmune destruction of pancreatic islet cells results in insulin deficiency, leading to type 1 diabetes mellitus (DM). Common presenting symptoms include polydipsia, polyphagia, weight loss, and polyuria (osmotic diuresis secondary to glycosuria).

18.2 What are the two types of this condition?

Type 1 DM is characterized by absolute insulin deficiency; type 2 DM is characterized by insulin resistance and increased insulin levels. type 1 DM typically presents in thin individuals younger than 30 years of age. type 2 DM typically affects obese individuals older than 30 years of age (although it is increasingly seen among younger obese individuals). Both types of diabetes can result in retinopathy, nephropathy, and neuropathy.

18.3 What is diabetic ketoacidosis (DKA)?

DKA is a life-threatening complication of uncontrolled type 1 DM. In the absence of insulin, increased levels of fatty acids are delivered to the liver, where ketogenesis occurs. this lowers the ph of the blood. presenting symptoms include Kussmaul

hyperpnea (deep respirations), abdominal pain, dehydration, and nausea/vomiting. patients may have a sweet/fruity/alcoholic odor to their breath.

18.4 What is the appropriate treatment for DKA?

Acute DKA requires rapid fluid resuscitation with normal saline, followed by the administration of intravenous insulin and repletion of depleted electrolytes, especially potassium. administration of bicarbonate to correct the acidic blood ph is usually not recommended unless the acidosis is severe. Following an episode of DKa, lifelong insulin replacement is required for patients diagnosed with type 1 DM. Oral hypoglycemic agents are effective in type 2 DM but not in type 1.

18.5 What electrolyte abnormalities are frequently associated with DKA?

DKA is associated with depletion of total body potassium stores through osmotic diuresis. Serum potassium levels may appear normal or elevated even though total body potassium stores are low; this is because intracellular potassium is shifted into the extracellular space in exchange for hydrogen ions to buffer the effects of metabolic acidosis. treatment of DKA with insulin drives potassium back into cells, and patients undergoing treatment for DKA can thus become profoundly hypokalemic.

19. A 14-year-old Hispanic-American boy with a family history of obesity and hypertension presents to the pediatrician for a mandatory school physical examination. He has no medical complaints. Social history is notable for a sedentary lifestyle. His diet consists of pizza, sandwiches, potato chips, and 2 cups of soda daily. Physical examination reveals a male with an abdominal circumference > 40 inches. His body mass index is 36 kg/m2, pulse is 100/min, and blood pressure is 140/95 mm Hg. Skin examination reveals velvety, darkly pigmented patches in the skin folds at the nape of his neck and axilla .

19.1 What is the most likely diagnosis?

Metabolic syndrome, also known as dysmetabolic syndrome, syndrome X, and insulin resistance syndrome.

19.2 What are the diagnostic criteria for this condition?

The National Cholesterol education program adult treatment panel III defines metabolic syndrome as the presence of any three of the following five traits: abdominal obesity (male > 40 inches; female > 35 inches); hypertriglyceridemia (≥ 150 mg/dL); low levels of high-density lipoprotein (HDL) cholesterol (male < 40 mg/dL; female < 50 mg/dL); blood pressure ≥ 130/85 mm hg; fasting glucose ≥ 110 mg/dL.

19.3 What do the skin findings represent?

Acanthosis nigricans is a common physical sign of insulin resistance, particularly in hispanics and african americans. It may be due to high levels of circulating insulin or insulin-like growth factor receptors in the skin. Other conditions with acanthosis nigricans include polycystic ovarian syndrome and some visceral malignancies.

19.4 What is insulin resistance?

Insulin resistance (Ir) is the state in which endogenous or exogenous insulin produces a less-than-expected biological effect. patients have elevated blood glucose with normal to elevated insulin levels. today, Ir is nearly universal in obese individuals and is correlated with amount of intra-abdominal fat. Several mechanisms of Ir in obesity have been proposed: insulin receptor downregulation; intracellular lipid accumulation; increased free fatty acids that impair insulin action; cytokines and "adipokines," which modify the effect of insulin. Treatment with metformin can be initiated to increase insulin responsiveness.

19.5 What class of drugs should be avoided in patients with this condition?

Atypical antipsychotics, such as clozapine, are associated with the metabolic syndrome, particularly weight gain and hypertriglyceridemia. even for patients without weight gain, the effect on serum triglycerides increases the risk for adverse cardiovascular events.

20. A 30-year-old African-American woman with a history of hypertension presents to her new primary care physician for a physical examination. She claims to be in good health but has noticed she is urinating more frequently and has had several urinary tract infections in the past year. Her family history is significant for premature coronary artery disease and diabetes in multiple first-degree relatives. Her heart rate is 70/ min and her blood pressure is 140/90mm Hg. Physical examination is notable for morbid obesity (body mass index: 48 kg/m2), and a urine dipstick reveals 2+ glycosuria.

20.1 What is the most likely diagnosis?

Non-insulin-dependent (type 2) diabetes mellitus (NIDDM).

20.2 What are the diagnostic criteria for this condition?

Random plasma glucose > 200 mg/dL with symptoms or Fasting plasma glucose > 126 mg/dL on two separate occasions or plasma glucose > 200 mg/dL 2 hours after a glucose tolerance test

20.3 What is the production and structure of insulin?

Insulin is originally produced as pre-proinsulin in the pancreas. During posttranslational processing, a signal peptide is removed, producing proinsulin. proinsulin contains two polypeptide chains connected by two sulfhydryl bonds (cysteine to cysteine) and a C-peptide. In the conversion from proinsulin (the zymogen) to active insulin, the C-peptide is cleaved off. Synthetic insulin lacks the C-peptide. therefore, measuring C-peptide is useful in patients in whom surreptitious insulin injection is suspected (factitious hypoglycemia).

20.4 How does insulin exert its effects on organs?

the insulin receptor is a heterodimer of α and β subunits. the β subunit is a tyrosine kinase. When insulin binds, this subunit autophosphorylates itself, leading to activation of downstream signaling cascades. Insulin stimulates glucose storage as glycogen in

the liver, triglyceride storage in adipose tissue, and amino acid storage as protein in muscle. It also promotes utilization of glucose in muscle for energy.

20.5 What is the most appropriate treatment for this patient?

The number one reason this patient has NIDDM is her obesity. therefore, nonpharmacologic treatments such as diet, weight reduction, and exercise must be employed. however, these have limited long-term success. pharmacologic treatment for type 2 DM includes oral hypoglycemic agents. Only in refractory cases is insulin added to the regimen. Tight glucose control markedly reduces microvascular and neurologic complications of DM. The goal is a hemoglobin A1C level of 7%.

21. A 36-year-old woman at 24 weeks' gestation presents to the clinic for a routine prenatal visit. Her fetus is large for gestational age, and she is scheduled for an oral glucose tolerance test (OGTT). She had one previous pregnancy with no complications and is obese but otherwise healthy. Results of the OGTT are as follows: 1-hour OGTT: glucose level 144 mg/dL 3-hour OGTT: fasting glucose level 97 mg/dL Glucose level at 1 hour: 210 mg/dL Glucose level at 2 hours: 190 mg/dL Glucose level at 3 hours: 143 mg/dL

21.1 What is the most likely diagnosis?

Gestational diabetes mellitus (DM) is defined as glucose intolerance first documented in pregnancy.

21.2 What is the pathophysiology of this condition?

Gestational DM occurs in approximately 4% of all pregnancies. Normal pregnancy is a diabetogenic (prodiabetic) state characterized by insulin resistance and decreased peripheral uptake of glucose. this is mediated by the production of counterregulatory (anti-insulin) hormones by the placenta, including human placental lactogen, cortisol, and placental growth hormone.

21.3 How is this condition diagnosed?

Gestational DM is most often asymptomatic and is usually detected at 24–28 weeks' gestation by a routine OGtt. In gestational DM, any two of the following levels are diagnostic: 1-hour postprandial glucose > 190 mg/dL, 2-hour postprandial glucose > 165 mg/dL, and/or 3-hour postprandial glucose > 145 mg/dL. Other signs include glycosuria, hyperglycemia, and fetus large for gestational age.

21.4 What risk factors are associated with this condition?

Risk factors include age < 25 years, family or past history of gestational DM, fetus large for gestational age, glycosuria at first prenatal visit, obesity, polycystic ovarian syndrome, previous stillbirths or abortions, maternal birthweight > 4.1 kg (9 lb), and hispanic or african american race.

21.5 What are the common fetal complications associated with this condition?

Common fetal complications include: congenital defects. Macrosomia. Perinatal mortality (2%–5%). Shoulder dystocia.

21.6 What are the appropriate treatments for this condition?

Affected women should adhere to a diabetic diet. Fasting blood glucose and 2-hour postprandial glucose levels should be routinely monitored. If levels remain high for 2 weeks, insulin therapy, rather than oral hypoglycemics, should be instituted. Fetal growth should also be monitored.

22. A worried mother brings her 12-year-old son to the pediatrician with concerns that he is "too tall." Both she and the patient's father are relatively short, as are other members of the family. The patient, an avid Little League player, complains only that his baseball cap, mitt, and shoes do not fit any more. on physical examination, the patient is above the growth curve for his age and has large hands and feet, frontal bossing of the cranium, prominent jaw, and coarse facial features with oily skin.

22.1 What is the most likely diagnosis?

Gigantism, which is caused by excess growth hormone (GH). In patients with fused epiphyses (ie, growth plates), the disease is called acromegaly. In older patients, physical changes may go unnoticed until hats, gloves, and shoes no longer fit.

22.2 What is the pathophysiology of this condition?

Excess Gh can arise from pituitary excess, hypothalamic Gh-releasing hormone (GHRH) excess, or an ectopic source. a genetic component of the disease is suggested by the high levels of GH seen in McCune-Albright syndrome and multiple endocrine neoplasia type I.

22.3 How is GH produced?

GH is produced and stored in the acidophilic cells of the anterior pituitary. Basophilic cells in the anterior pituitary can be recalled with the mnemonic B-FLAT. Basophils: Follicle-stimulating hormone, Luteinizing hormone, Adrenocorticotropic hormone, and Thyroid-stimulating hormone. acidophils: Gh and prolactin.

22.4 How is secretion of GH controlled?

GH is released in a pulsatile fashion. Secretion is controlled by the hypothalamus. GHRH stimulates GH production. Somatostatin interferes with its effect on the pituitary. Insulin-like growth factor-1 (IGF-1) exerts negative feedback to inhibit GH secretion. at puberty, the frequency and amplitude of GH secretory pulses increase because of gonadal hormones. the combination drives the "growth spurt."

22.5 How is this condition diagnosed?

Excess GH production is diagnosed by physiologic testing and brain imaging. Screening: the best screening test for excess GH secretion is a measurement of serum IGF-1 levels. IGF-1 levels are a more reliable indicator of GH excess than GH levels because IGF-1 remains constant throughout the day whereas Gh fluctuates. IGF-1 levels are elevated in acromegaly and gigantism because IGF-1 synthesis is dependent on GH. Confirmatory test: the diagnosis of GH excess can be confirmed with an oral glucose suppression test. In normal patients, GH levels are suppressed after the

administration of a glucose load. In patients with gigantism or acromegaly, GH values may rise, remain unchanged, or suppress only partially.
Imaging: MRI of the pituitary gland may reveal adenoma as the source of excess GH secretion.
26. A patient complains of headaches and visual disturbances. A casual glance reveals that the patient's finger bones are enlarged in diameter, a heavy deposition of bone exists over the eyes, and the patient has a prominent jaw. The doctor tells you that the headaches and visual disturbances result from increased pressure within the skull and that the patient is suffering from a pituitary tumor that is affecting hormone secretion. Name the hormone that is causing the problem, and explain the increase in pressure and the visual disturbances.

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