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USMLE STEP 1

United State Medical Licensing Examination

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Sections

1. Anatomy
2. Physiology
3. Biochemistry
4. Microbiology/Immunology
5. Pathology and Path physiology
6. Pharmacology
7. Behavioral Science and Biostatics

step 1

QUESTION 1
In the skull, a network of thick-walled vessels named dural venous sinuses drains the cerebrospinal fluid and the venous blood from the brain. These vessels are formed by reflections of the dura mater, which also form partitions between major parts of the brain. Which of the following dural venous sinuses is associated with the falx cerebri?

A. cavernous sinus
B. inferior petrosal sinus
C. sigmoid sinus
D. superior sagittal sinus
E. transverse sinus

Correct Answer: D
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The falx cerebri is the dural partition separating the hemispheres of the brain, above the corpus callosum. It has in its superior edge the superior sagittal sinus and in its inferior border, the inferior sagittal sinus. The cavernous sinus (choice A) is a dural pocket in the middle cranial fossa and is located on either side of the sella turcica. It is unusual because it contains the internal carotid artery and cranial nerves III, IV, V1, V2, and VI. The sigmoid sinus (choice C) is located in the posterior cranial fossa, below the level of the tentorium cerebelli, which contains in its posterior border the transverse sinus (choice E).

QUESTION 2
A patient was thrown from a tractor, which partially ran over him and caused injury to the base of the skull. The origin of the internal jugular vein at the jugular foramen was compromised. Which of the following cranial nerves courses through the jugular foramen?

A. abducens (sixth cranial) nerve
B. facial (seventh cranial) nerve
C. hypoglossal (twelfth cranial) nerve
D. spinal accessory nerve (eleventh cranial) nerve
E. vestibulocochlear (eighth cranial) nerve

Correct Answer: D
Section: Anatomy
Explanation

Explanation/Reference:

Explanation:
The spinal accessory (eleventh cranial) nerve takes its origins in the neck, but then runs cranially into the skull through the foramen magnum to join with its cranial component. They exit as one through the jugular foramen, along with the glossopharyngeal (ninth cranial) and vagus (tenth cranial) nerves. The abducens (sixth cranial) nerve (choice A) runs through the superior orbital fissure to reach the orbit. The facial (seventh cranial; choice B) and vestibulocochlear (eighth cranial; choice E) nerves run together through the internal acoustic meatus into the temporal bone. The facial nerve exits the skull through the stylomastoid foramen. The hypoglossal (twelfth cranial; choice C) nerve exits the skull through the hypoglossal canal.

QUESTION 3
Protein zero (P0) is the predominant protein in myelin in the peripheral nervous system and its function is to stabilize adjacent plasma membranes by interaction with similar P0 molecules. Which of the following cells manufacture P0?

A. fibrous astrocytes
B. microglia
C. oligodendrocytes
D. protoplasmic astrocytes
E. Schwann cells

Correct Answer: E
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
Schwann cells produce myelin in the peripheral nervous system whereas oligodendrocytes produce myelin in the central nervous system. Oligodendrocytes manufacture the proteolipid protein, the functional equivalent to P0 in the central nervous system. Fibrous (choice A) and protoplasmic (choice D) astrocytes are supportive cells which play a role in the regulation of brain metabolism. Microglia (choice B) are mesodermal in origin and have phagocytotic activity in the central nervous system.

QUESTION 4
Aperilunate fracture dislocation is a devastating closed injury of the wrist. It usually results from a fall where the weight of the body is transferred onto the wrist. The hand is caught in the hyperextended and ulnar deviated position. The fracture dislocation involves rupture of interosseous ligaments, joints, and ultimately dislocation/fracture of the lunate bone. In the anatomical position, which carpal bone lies directly distal to the lunate?

A. capitates
B. hamate
C. scaphoid
D. trapezoid
E. triquetrum

Correct Answer: A
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The capitate bone lies directly distal to the lunate. The mechanism of perilunate fracture dislocation involves rupture of the radioscaphocapitate and scapholunate interosseous ligaments, dislocation of the capitolunate joint, rupture of the lunotriquetral interosseous ligament, and finally dislocation/rupture of the lunate. In the anatomical position, the hamate (choice B) is the most medial carpal bone, located just distal to the triquetrum. The scaphoid (choice C) lies lateral to the lunate and proximal to the trapezium (choice D), the carpal bone articulating with the thumb. The trapezoid (choice E) is medial to the trapezoid and distal to the scaphoid. The lunate bone (choice C) lies adjacent to the scaphoid in the proximal row of carpals and with the scaphoid articulates with the radius at the radiocarpal or wrist joint. It is not related to the anatomic snuffbox. The pisiform bone (choice D) is a sesamoid bone in the tendon of the flexor carpi ulnaris on the lateral wrist. It is not related to the anatomic snuffbox.

QUESTION 5
A 19-year-old man was in a barroom brawl and was punched squarely in the right eye. He comes to the emergency room the next day and complains of diplopia. An X-ray reveals fracture of the orbital floor. Neurological examination shows loss of sensation of the skin of the right face below the right eye and the upper gums. Which of the following nerves may be injured?

A. frontal nerve
B. infraorbital nerve
C. nasociliary nerve
D. supraorbital nerve
E. trochlear nerve

Correct Answer: B
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The infraorbital nerve, a branch of the maxillary (V2) division of the trigeminal (fifth cranial) nerve, courses below the orbital floor to reach the area of skin below the

eye. It provides superior alveolar branches to supply the upper gums and is vulnerable in fractures involving the floor of the orbit and face area. All the nerves mentioned in the other choices will be spared by this type of injury. The frontal nerve (choice A) and nasociliary nerve (choice C) are branches from the ophthalmic division (V1) of the trigeminal (fifth cranial) nerve and course within the orbit. The supraorbital (choice D) nerve is a continuation branch of the frontal nerve onto the forehead, providing sensory innervation for this area. The trochlear (fourth cranial) nerve is also located within the orbit.

QUESTION 6
Cells in the pancreas that secrete glucagon and insulin are which of the following?

A. A and B cells
B. acinar cells
C. D cells
D. pancreatic D1 cells
E. pancreatic polypeptide cells

Correct Answer: A
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
In the human pancreas, A and B cells of the islets of Langerhans secrete glucagon and insulin, respectively. Pancreatic D1 cells (choice D) release a product similar to vasoactive intestinal polypeptide. Pancreatic polypeptide cells (choice E) secrete pancreatic polypeptide and D cells (choice C) release somatostatin. All the aforementioned cells belong to the endocrine pancreas. Acinar cells (choice B) are part of the exocrine pancreas and do not secrete glucagon or insulin.

QUESTION 7
Below figure is a high magnification photomicrograph of the gall bladder. The arrow points to the internal lining that is formed by which of the following?

A. pseudostratified columnar epithelium
B. simple columnar epithelium
C. stratified cuboidal epithelium
D. stratified squamous epithelium
E. transitional epithelium

Correct Answer: B
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:

The lining of the gallbladder is a simple columnar epithelium identifiable by tall cells with elongated nuclei arranged at the same level. Pseudostratified epithelium (choice A) is distinguishable from the simple columnar epithelium by the cell nuclei being arranged at different levels. Stratified cuboidal epithelium (choice C) is characterized by short cells with nuclei arranged at different levels. Stratified epithelium (choice D) has a characteristic cellular basal layer with flat degenerate cells in its upper layer. Transitional epithelium (choice E) is a type of stratified epithelium exclusively confined to the urinary tract.

QUESTION 8
During surgery at the root of the neck, an attending surgeon cautions her resident to locate important structures which need to be protected. One of these is the phrenic nerve, responsible for the innervation of the diaphragm and thus, respiration. The phrenic nerve can be positively identified by which of the following anatomical relationships?

A. It is found immediately between the common carotid artery and the internal jugular vein.
B. It lies immediately between the esophagus and the trachea.
C. It lies on the scalenus medius muscle.
D. It wraps around the right subclavian artery.
E. The suprascapular and transverse cervical arteries cross over it anteriorly.

Correct Answer: D
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
At the root of the neck, the phrenic nerve (C3, C4, C5) lies on the scalenus anterior muscle, not the scalenus medius (choice C). The transverse cervical and suprascapular arteries course over it. The vagus (tenth cranial) nerve, not the phrenic nerve is located between the common carotid artery and the internal jugular vein (choice A). The recurrent laryngeal branch from the vagus nerve wraps around the right subclavian artery (choice D), and courses cranially between the esophagus and the trachea (choice B).

QUESTION 9
A premature female infant is born about 24 weeks after fertilization and develops rapid, labored breathing shortly after birth. She is immediately transferred to intensive care where she is diagnosed with hyaline membrane disease (HMD). Which of the following is most likely deficient in the infant?

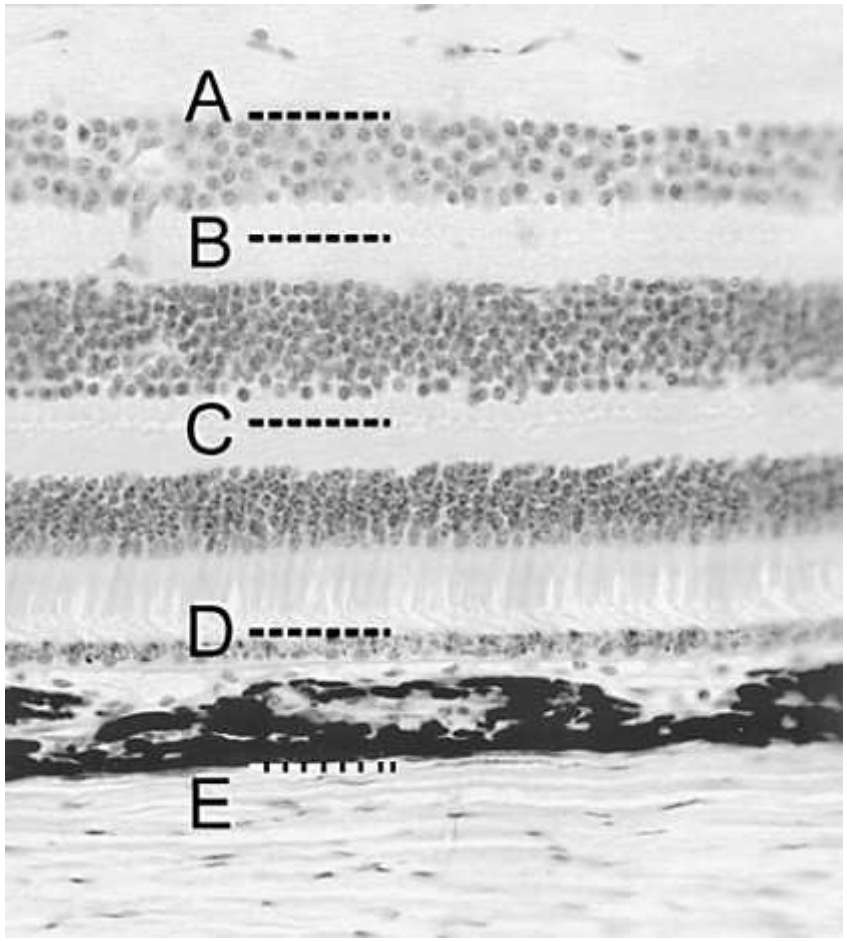
A. alveolar ducts
B. lung surfactant
C. terminal saccules
D. type I alveolar cells
E. type II alveolar cells

Correct Answer: D
Section: Anatomy

Explanation

Explanation/Reference:
Explanation:
HMD is also known as respiratory distress syndrome, which is most often caused by the lack of lung surfactant, due to a premature birth. Lung surfactant production begins around 20 weeks after fertilization. But it is present only in small amounts until the last 2 weeks before birth when its amount increases significantly. Alveolar ducts (choice A) branch from the respiratory bronchioles during development. Type I alveolar cells (choice D) or pneumocytes are squamous epithelial cells, which participate in gas exchange. These epithelial cells line the terminal saccules (choice C). Type II alveolar cells (choice E) synthesize surfactant.

QUESTION 10
Which label in following figure indicates the typical plane of separation at which retinal detachment occurs?



A. A
B. B
C. C
D. D
E. E

Correct Answer: D
Section: Anatomy

Explanation

Explanation/Reference:
Explanation:
Retinal separation typically occurs at the interface between the retinal pigment epithelium and the outer limit of the sensory (neural) retina. The weakness of this plane is attributed to the manner in which the retina develops, a process that involves obliteration of the space between two of the layers of the optic cup--an inner layer from which the sensory retina arises and an outer layer from which the retinal pigment epithelium arises. Other retinal layers are bridged by neuronal processes, and Müller cells (the retina's glial cells) span the entire thickness of the neural retina. Plane A(choice A) marks the boundary between the nerve fiber layer above and the ganglion cell layer below. The nerve fiber layer is composed of axons of the retinal ganglion cells. Plane B (choice B) is within the inner plexiform layer, the site of synaptic contacts between bipolar neurons, retinal ganglion cells, and amacrine cells. Plane C (choice C) is within the outer plexiform layer, the site of synapses among bipolar cells, rods and cones, and horizontal cells. The boundary between the choroid (of the middle vascular tunic or uvea) and the sclera (of the external, fibrous tunic) is marked by plane E (choice E).

QUESTION 11
A 28-year-old male patient suffering from head trauma resulting from a car accident is brought unconscious to the emergency room. In performing the pupillary light reflex, you notice that even though the left pupil constricts when you shine a light directly into the left eye, it does not do so when you shine a light into the right eye. This is best explained by a disconnection between which of the following bilateral structures?

A. Edinger-Westphal nucleus
B. habenula
C. inferior colliculus
D. lateral geniculate nucleus
E. medial geniculate nucleus

Correct Answer: A
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The central visual pathway for the papillary light reflex is organized as follows: fibers from the ganglionic layer of the retina project posteriorly to the pretectum, which in turn innervates the Edinger- Westphal nucleus. Preganglionic parasympathetic neurons in the Edinger- Westphal nucleus project to the ciliary ganglion, which sends postganglionic parasympathetic innervation back to the constrictor pupillae of the eye. The Edinger-Westphal nuclei from each side of the midbrain are also connected to each other by projections running through the posterior commissure. Disconnection of these fibers will result in loss of the consensual papillary light reflex on the contralateral side, as happens in this case. The habenula (choice B) is a nucleus of the thalamus, which does not participate in the central visual pathways. The lateral geniculate nucleus (choice D) receives fibers from the ganglionic layer of the retina. However, fibers participating in the papillary light reflex run through this structure without synapsing and terminate in the pretectum. Thus, the lateral geniculate nucleus does not participate in the pupillary light reflex. The inferior colliculus (choice C) and the medial geniculate nucleus (choice E) are components of the auditory system.

QUESTION 12
A 45-year-old female patient presents to the emergency room with a headache and complains of abnormal sensations on the left side of her body. She claims that

the sensory changes came on rapidly in the last few hours. Her laboratory reports come back normal, a spinal tap reveals normal cerebrospinal fluid (CSF), and her mental ability seems good. You perform a neurological examination and find she has greatly reduced sensation on the entire left side of her body, including her face. The sensory loss includes all modalities. The motor examination is normal, as is her visual examination and hearing examination. Based on the neurological findings, which of the following thalamic nuclei would be involved?

A. lateral and medial geniculate nuclei
B. lateral dorsal and lateral posterior nuclei
C. pulvinar
D. ventral anterior and ventral lateral nuclei
E. ventral posterior lateral and ventral posterior medial nuclei

Correct Answer: E
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The ventral posterior lateral (VPL) and ventral posterior medial (VPM) nuclei are sensory relay thalamic nuclei. The lateral and medial geniculate nuclei (choice A) are respectively concerned with visual and auditory sensory information. The lateral dorsal (LD) and lateral posterior (LP) nuclei (choice B), and the pulvinar (choice C) are association or multimodal relay nuclei. The ventral anterior (VA) and ventral lateral (VL) are motor relay nuclei.

QUESTION 13
A patient has been admitted for hematemesis (vomiting of blood). Endoscopic examination reveals bleeding esophageal varices resulting from portal obstruction. These varices represent anastomoses between branches of which of the following?

A. inferior vena cava with a patent ductus venosus
B. left gastric, azygos, and hemiazygos veins
C. right gastric vein and the inferior vena cava
D. superior, middle, and inferior rectal veins
E. veins running on the ligamentum teres and the epigastric veins

Correct Answer: B
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
Obstruction of the portal vein results in an increase in the collateral circulation between veins that normally drain to the portal vein and those that drain to the systemic veins. Choices A, B, D, and E all represent possible collateral venous circulation in case of portal obstruction. Choice Ais rare because the ductus

venosus closes after birth. Choice B is correct because varicose veins in this region give rise to esophageal varices. Choice D results in varicose veins in the rectal region. Choice C is incorrect because there is no connection between the right gastric vein and the inferior vena cava. In choice E, enlargement of the epigastric veins results in varicose veins radiating from the umbilicus, the caput medusae.

QUESTION 14
A 15-year-old high school football player is brought to the emergency room. On examination, his right lower limb is deformed and swollen around the knee. At full extension, there is valgus instability, suggestive of knee dislocation. The patient is in great pain and there is a concern for concomitant vascular and nervous injuries. Palpation of the dorsalis pedis artery reveals a normal pulse. However, neurological examination reveals impaired dorsiflexion of the foot with decreased sensation in the space between digits 1 and 2. Which of the following nerves is affected?

A. deep peroneal (fibular) nerve
B. femoral nerve
C. saphenous nerve
D. superficial peroneal (fibular) nerve
E. tibial nerve

Correct Answer: A
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The deep peroneal (fibular) nerve innervates the muscles responsible for dorsiflexion in the anterior compartment of the leg. It also provides for the cutaneous innervation of the space between digits 1 and
2. The femoral nerve (choice B) innervates muscles in the anterior compartment of the thigh and the skin of the medial aspect of the leg by a continuing branch, the saphenous nerve (choice C). The superficial peroneal (fibular) nerve (choice D) innervates the lateral compartment of the leg and muscles responsible for foot eversion. The tibial nerve (choice E) innervates the posterior compartment of the leg and the muscles responsible for plantar flexion.

QUESTION 15
In the central auditory pathways, second-order neurons are located in which of the following?

A. cochlear (spiral) ganglion
B. cochlear nuclei
C. inferior colliculi
D. nuclei of lateral lemniscus
E. superior olivary nuclei

Correct Answer: B
Section: Anatomy

Explanation

Explanation/Reference:
Explanation:
Second-order neurons in the central auditory pathways are located in the dorsal and ventral cochlear nuclei. They receive afferents from the first-order neurons located in the cochlear (spiral) ganglion (choice A). Secondorder fibers from the cochlear nuclei project in turn to the inferior colliculi (choice C), nuclei of lateral lemniscus (choice D), and superior olivary nuclei (choice E).

QUESTION 16
Arrow 2 in following figure points to which of the following structures?

A. glomerulus
B. juxtaglomerular cells
C. lacis cells
D. macula densa
E. vascular pole of the renal corpuscle

Correct Answer: D
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The macula densa indicated by arrow 2 is a modified segment of the distal tubule at the site of its passage adjacent to the vascular pole of the renal corpuscle. The name arises from the close spacing of nuclei of the epithelial cells forming this part of the distal tubule. These cells are thought tosense the chloride content in the passing filtrate and generate signals that regulate the caliber of the afferent arteriole. The glomerulus (choice A, arrow 1) is a network of capillaries derived from the afferent arteriole and suspended within Bowman's capsule by its vascular pole. The juxtaglomerular cells (choice B) form a cuff around the afferent arteriole prior to its entrance into the glomerulus and they secrete renin. Lacis cells (choice C, arrow 4) are extraglomerular mesangial cells with an uncertain function. The vascular pole (choice E, arrow 3) feeds blood to the glomerulus and carries blood away from it. As part of the juxtaglomerular apparatus, it is closely apposed to the macula densa.

QUESTION 17
A gang member is rushed to the emergency room suffering from multiple stab wounds made by an ice pick. Athird-year medical student rotating through emergency medicine is puzzled by the sight of a milky white substance exuding from a stab wound just superior to the right sternoclavicular joint. Which of the following structures is possibly injured at this location?

A. the common carotid artery
B. the cupola of the right lung
C. the internal jugular vein
D. the right lymphatic trunk

E. the thoracic duct

Correct Answer: D
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The right lymphatic trunk is ruptured and chyle is exuding from the wound. Blood would flow from a wound involving the common carotid artery (choice A) or internal jugular vein (choice C). Astabbing lesion of the cupola of the right lung (choice B) would result in pneumothorax. The thoracic duct (choice E) does carry chyle. However, the thoracic duct drains into the bifurcation of the internal jugular and subclavian veins on the left side, above the left sternoclavicular joint.

QUESTION 18
A 72-year-old male patient has suffered a cerebral infarct affecting the left cerebral hemisphere. On examination of the patient, it is noticed that his verbal output is fluent and paraphasic. His comprehension of speech is normal but repetition is severely impaired. Naming is also impaired, although when given a list, the patient is able to select the correct name. Special consultation with a neurologist results in a diagnosis of conduction aphasia. Which of the following brain structures is affected?

A. arcuate fasciculus
B. Broca's area
C. nucleus ambiguous
D. red nucleus
E. Wernicke's area

Correct Answer: A
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The arcuate fasciculus connects Wernicke's area to Broca's area, integrating comprehension of speech with motor speech. A lesion in this connecting bundle results in this unusual condition of conduction aphasia, characterized by impairment of repetition and naming. Broca's area (choice B) is the motor speech area and lesion in this area will result in motor speech impairment. However, this patient's verbal output is fluent. Alesion in the nucleus ambiguus (choice C) will result in dysarthria and also loss of a fluent verbal output. The red nucleus (choice D) is a mesencephalic motor nucleus, which does not participate in the central pathways for speech. Wernicke's area (choice E) is the speech comprehension area, which is intact in this patient because he comprehends spoken language.

QUESTION 19
Which of the following is characterized by an absence of lymphoid follicles and germinal centers?

A. axillary lymph node

B. Peyer's patches
C. pharyngeal tonsil
D. spleen
E. thymus

Correct Answer: E
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The thymus provides for development of new T lymphocytes in an environment shielded from foreign antigens. Like bone marrow, the thymus is a primary lymphoid organ, and not a site of reactions to foreign antigens. Lymphoid follicles are sites of B lymphocyte proliferation in response to antigen stimulation. These occur in the lymph nodes (choice A), Peyer's patches (choice B), tonsils (choice C), and white pulp of the spleen (choice D).

QUESTION 20
A 24-year-old student is brought to the emergency room after being found in a ditch where he had lain overnight after being hit by a car. He complains of severe pain in the left arm and examination reveals a broken humerus. Neurological examination reveals that the patient can extend the elbow but displays inability to supinate the elbow when it is extended. The patient also has wrist drop and very weak hand grasp. The neurological lesion is likely localized at which of the following locations?

A. posterior cord of the brachial plexus
B. posterior divisions of the brachial plexus
C. radial nerve at the distal third of the humerus
D. radial nerve at the midforearm
E. radial nerve at the wrist

Correct Answer: C
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
Wrist drop and weak hand grasp indicate that the patient has a lesion of the radial nerve, most likely at the distal third of the humerus, sparing the innervation of the tríceps brachii but affecting the supinator. Because the patient can extend the elbow, the integrity of the posterior cord (choice A) and posterior divisions (choice B) of the brachial plexus is preserved. Lesion of the radial nerve at the midforearm (choice D) and wrist (choice E) would spare the innervation of the supinator.

QUESTION 21
A 24-year-old student is brought to the emergency room after being found in a ditch where he had lain overnight after being hit by a car. He complains of severe

pain in the left arm and examination reveals a broken humerus. Neurological examination reveals that the patient can extend the elbow but displays inability to supinate the elbow when it is extended. The patient also has wrist drop and very weak hand grasp. The neurological lesion is likely localized at which of the following locations? In the above patient, when the elbow is partially flexed, the patient can supinate the left forearm. This is due to the function of which of the following?

A. biceps brachii
B. brachialis muscle
C. brachioradialis
D. pronator teres
E. anconeus

Correct Answer: A
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The biceps brachii is a strong supinator of the forearm through its attachment to the radial tuberosity, but it can only function when the elbow is partially flexed. The supinator by itself is a weaker supinator muscle: prove it to yourself by using a screwdriver with your right elbow flexed (biceps brachii and supinator) and your right elbow extended (supinator only). The brachialis (choice B) and brachioradialis (choice C) muscles are flexors of the forearm. The pronator teres (choice D), as its name indicates, pronates the forearm. The anconeus (choice E) helps in extension of the elbow.

QUESTION 22
Hormone-secreting chromophils in the pars distalis of the adenohypophysis are classified into acidophils and basophils. Which of the following hormones is secreted by the acidophils?

A. adrenocorticotropin
B. follicle-stimulating hormone
C. luteinizing hormone
D. prolactin
E. thryrotropin (thyroid-stimulating hormone)

Correct Answer: D
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
Prolactin is secreted by one of the two types of hormone-secreting acidophils, the mammotrophs. The other types of acidophils are the somatotrophs, which

secrete growth hormone (somatotropin). The hormones listed in all the other choices are secreted by the basophils. Adrenocorticotropin (choice A) is secreted by the corticotrophs. The gonadotrophs secrete either follicle-stimulating hormone (choice B) or luteinizing hormone (choice C). Thyrotropin (choice E) is secreted by thyrotrophs.

QUESTION 23
Production of specific granules occurs mainly during which stage of granulocyte development?

A. granulocyte colony-forming unit
B. metamyelocyte
C. myeloblast
D. myelocyte
E. promyelocyte

Correct Answer: D
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
Generation of specific granules occurs during the myelocyte stage. Development of all three types of granulocytes follows a similar sequence of stages. The granulocyte colonyforming unit (choice A) is an undifferentiated progenitor cell of the granulocyte line. Buildup of the protein synthesis machinery occurs during the myeloblast (choice C) and promyelocyte (choice E) stages. The promyelocyte stage is also characterized by production of primary (nonspecific) granules. After the myelocyte stage, further condensation and reshaping of the nucleus occurs during the metamyelocyte stage (choice B).

QUESTION 24
A 1-year-old infant presents with cardiomegaly and congestive heart failure. She has increased intracranial pressure with hydrocephaly and cranial bruit. A vein of Galen aneurysm, revealed by MRI, is shown to compress the aqueduct of Sylvius, the posterior part of the third ventricle, and the splenium of the corpus callosum. Normally, the cerebral vein of Galen joins with which dural venous sinus?

A. inferior sagittal sinus
B. sigmoid sinus
C. superior petrosal sinus
D. superior sagittal sinus
E. transverse sinus

Correct Answer: A
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The great cerebral vein of Galen joins with the inferior sagittal sinus to form the straight sinus. The latter drains into the transverse sinus (choice E). The superior sagittal sinus (choice D) drains posteriorly into the transverse sinus. The transverse sinus which runs bilaterally on the posterior wall of the posterior cranial fossa becomes the sigmoid sinus (choice B) which flows into the internal jugular vein. The superior petrosal sinus (choice C) extends from the cavernous sinus to the beginning of the sigmoid sinus.

QUESTION 25
A newborn female infant cannot swallow, exhibits persistent drooling, and aspiration or regurgitation of food after attempted feedings. When the infant strains, coughs, or cries, the stomach inflates, elevating the diaphragm and making respiration more difficult. The patient is diagnosed with congenital esophageal atresia at the cervical levels, necessitating surgical repair. During the surgery, the blood supply of the esophagus must be carefully isolated to protect from injury. Which of the following arteries supplies the esophagus at cervical levels?

A. bronchial artery
B. inferior thyroid artery
C. internal thoracic artery
D. left inferior gastric artery
E. left inferior phrenic artery

Correct Answer: B
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The inferior thyroid artery provides for the majority of the blood supply of the esophagus at cervical levels. It can be assisted by branches from the common carotid, subclavian, vertebral, ascending pharyngeal, superficial cervical, and costocervical arteries. The bronchial arteries (choice A) supply the thoracic portion of the esophagus and maybe assisted in the lower part by branches of the internal thoracic artery (choice C). The abdominal portion of the esophagus is vascularized by branches from the left inferior gastric artery and left inferior phrenic artery.

QUESTION 26
During development, the upper limb buds appear by day 27 and the lower limb buds by day 29. An apical ectodermal ridge at the tip of each limb bud promotes

growth. This multilayered epithelial structure interacts with which of the following to direct the growth of the limb?

A. ectoderm
B. endoderm
C. mesenchyme
D. notochord
E. sclerotome

Correct Answer: C
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The apical ectodermal ridge secretes fibroblast growth factors, which act on mesenchymal cells in the zone of polarizing activity at the posterior margin of the limb bud. Activation of the zone of polarizing activity causes expression of the sonic hedgehog gene. Proteins expressed by the sonic hedgehog gene control the anteroposterior developmental pattern of the limb. The apical ectodermal ridge is contained within the ectoderm (choice A) and has no interaction with the endoderm (choice B). The notochord (choice D) and sclerotome (choice E) are structures involved in the development of the axial skeleton and not the limbs.

QUESTION 27
Serous cells are glandular acinar cells that produce a watery, proteinaceous fluid. This cell type is most predominant in which of the following glands?

A. esophageal glands
B. intestinal glands (of Lieberkün)
C. the parotid gland
D. the sublingual gland
E. the submandibular gland

Correct Answer: C
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The parotid gland is the only major salivary gland containing almost exclusively serous secretory cells. Esophageal (choice A) and intestinal glands (choice B) are small mucus-secreting glands. The sublingual (choice D) and submandibular glands (choice E) are mixed glands with differing proportions of serous and mucous cells.

QUESTION 28

Amember of a college fraternity, who had consumed a large amount of alcohol on a dare, is brought to the emergency room with vomiting and severe abdominal pain. Blood tests reveal that he has elevated serum levels of amylase and lipase. Atentative diagnosis of acute hemorrhagic pancreatitis is formulated. Which cells of the pancreas are directly involved in this condition?

A. alpha cells
B. beta cells
C. centroacinar cells
D. delta cells
E. F cells

Correct Answer: C
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
Centroacinar cells are components of the exocrine pancreas and they contain zymogen granules, which are released under the action of cholecystokinin from the duodenum. The zymogen granules contain inactive proenzymes that normally become activated within the duodenum. Premature activation of the pancreatic enzymes, such as trypsin, leads to autodigestion of the centroacinar cells of the pancreatic acini, which secrete these enzymes. This results in acute hemorrhagic pancreatitis which can be caused by excessive alcohol ingestion. All the other choices are cells of the endocrine pancreas, which secrete hormones. Alpha cells (choice A) secrete glucagon whereas beta cells (choice B) produce insulin. Delta cells (choice C) synthesize gastrin and somatostatin. F cells produce pancreatic polypeptide.

QUESTION 29
A football player was simultaneously tackled from the front above the knee and from the back below the knee. In the emergency room, he displays a positive anterior drawer test which becomes negative if the knee is internally or externally rotated. Which of the following has ruptured?

A. anterior cruciate ligament
B. fibula
C. fibular (lateral) collateral ligament
D. posterior cruciate ligament
E. tibial (medial) collateral ligament

Correct Answer: A
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:

In the anterior drawer test, the patient's tibia is pulled forward and anterior tibial displacement reveals rupture of the anterior cruciate ligament. The drawer test becomes negative when the knee is internally rotated because of the tightening of the posterior cruciate ligament (choice D); in this case, the result reveals that the posterior cruciate ligament is not affected. External rotation is limited by the tibial (medial) collateral ligament (choice E) and since the drawer sign is negative with the knee in this position, this ligament is also intact. The fibula (choice B) and fibular colateral ligament (choice C) do not participate in the knee joint and have no effect on the drawer test.

QUESTION 30
In this same patient, the pectineus muscle is also badly bruised. This muscle is innervated by which of the following?

A. genitofemoral nerve
B. obturator nerve
C. peroneal division of the sciatic nerve
D. saphenous nerve
E. tibial division of the sciatic nerve

Correct Answer: B
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The pectineus muscle is part of the adductor muscles of the thigh, which are innervated as a group by the obturator nerve. The genitofemoral nerve (choice A) provides sensory innervation for a small area of the skin in the medial superior aspect of the thigh, and motor innervation to the cremaster muscle. The peroneal division of the sciatic nerve (choice C) innervates the skin and muscles in the peroneal and anterior comparments of the leg. The saphenous nerve (choice D) is purely a sensory nerve for the medial aspect of the leg and the foot. The tibial division of the sciatic nerve (choice E) provides sensory and motor innervations to the posterior compartment of the leg and the plantar foot.

QUESTION 31
An overworked surgical resident is resecting an acinic cell carcinoma from the inferior aspect of the parotid gland when he makes a careless incision and nicks a branch of the facial (seventh cranial) nerve. Which of the following muscles may be affected by this injury?

A. omohyoid
B. sternohyoid
C. sternothyroid
D. stylohyoid
E. thyrohyoid

Correct Answer: D
Section: Anatomy

Explanation

Explanation/Reference:
Explanation:
The stylohyoid is innervated by the facial (seventh cranial) nerve. During the embryonic period, the muscles developing from the second pharyngeal arch include the stylohyoid, stapedius, posterior belly of the digastric, auricular muscles, and muscles of facial expression. The nerve supplying the second pharyngeal arch, and thus all these muscles, is the facial (seventh cranial) nerve. All the other muscles, omohyoid (choice A), sternohyoid (choice B), sternothyroid (choice C), and thyrohyoid (choice E) form the infrahyoid muscle. They are supplied as a group by branches of the ansa cervicalis derived from C1, C2, and C3.

QUESTION 32
A 35-year-old male patient suffering from pulmonary hypertension has been diagnosed with ostium secundum atrial septal defect. Abnormal development of which of the following structures is responsible for this developmental defect?

A. aorticopulmonary septum
B. endocardial cushion
C. interventricular septum
D. septum primum
E. sinus venosus

Correct Answer: D
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
Abnormal development of either the septum primum or septum secundum results in ostium secundum atrial septal defects in the area of the fossa ovalis. This common type of congenital heart defect is manifested by a patent foramen ovale between right and left atria. This is well-tolerated during childhood, but symptoms usually appear after 30 years of age. The aorticopulmonary septum (choice A) divides the truncus arteriosus of the developing heart and gives rise to the ascending aorta and pulmonary trunk. The endocardial cushions (choice B) give rise to the right and left atrioventricular canals. The interventricular septum (choice C) forms between the right and left ventricles. The sinus venosus (choice E) becomes incorporated into the atria, as well as giving rise to the openings of the pulmonary veins and the venae cavae.

QUESTION 33
Desmin is a 53-kDa protein found in skeletal and smooth muscle cells. It plays a role in coordinating muscle cell contraction. Desmin belongs to which type of intermediate filaments?

A. type I
B. type III
C. type IV
D. type V

E. type VI

Correct Answer: B
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
Desmin belongs to the type III intermediate filaments. Intermediate filament proteins have three domains: a head domain (N-terminal), an alpha-helical rod domain, and a tail domain (C-terminal). The six types of intermediate filament proteins are differentiated by the sequence in the rod domain. Type I (choice A) intermediate filaments include the cytokeratins. Type IV (choice C) intermediate filaments are found in the nervous system and include the neurofilaments and alpha-internexin. Type V (choice D) intermediate filaments are the nuclear lamins. Nestin, expressed in stem cells of the central nervous system, is a type VI (choice E) intermediate filament.

QUESTION 34
Which of the following normally occupy the dark spaces indicated by the arrows in following figure?

A. blood vessels
B. differentiating blood cell precursors
C. osteoblasts
D. osteoclasts
E. osteocytes

Correct Answer: E
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The black areas in this section of dried, compact bone are empty spaces normally occupied by cells and soft tissues. The arrows indicate lacunae interspersed among lamellae of osteons (haversian systems). In life, these are occupied by osteocytes. The fine lines radiating from the lacunae are canaliculi, which contain processes of the osteocytes. Blood vessels (choice A) of compact bone course through Volkmann's canals (not shown) and haversian canals (seen here at the center of each osteon). Hematopoietic cells (choice B) occur in red marrow located within medullary canals of long bones and the cavities of cancellous bone. Osteoblasts (choice C) are restricted to surfaces of bone at sites of bone apposition. When osteoblasts become entrapped in lacunae as a result of their synthetic activity, they become osteocytes. Osteoclasts (choice D) are large, multinucleated cells found at surfaces of bone at sites that are undergoing absorption.

QUESTION 35
A 19-year-old camper fell asleep with the right side of her face against the cold earth on an autumn night. In the morning, she woke up and found that she could not move the right side of the face. She went to the local emergency room in a nearby town and was diagnosed with Bell's palsy. Which of the following muscles is not affected in her condition?

A. buccinators
B. levator labii superioris
C. levator labii superioris alaeque nasi
D. levator palpebrae superioris
E. orbicularis oculi

Correct Answer: D
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The levator palpebrae superioris, which opens the upper eyelid and is located in the orbit, is innervated by the oculomotor (third cranial) nerve. In this case of Bell's palsy, longterm exposure to the cold has affected the peripheral portion of the facial (seventh cranial) nerve. The buccinator (choice A), levator labii superioris (choice B), levator labii superioris alaeque nasi (choice C), and orbicularis oculi (choice E) are all innervated by the facial nerve and will all be impaired.

QUESTION 36
In examining a 30-year-old male patient with multiple sclerosis, you notice that when you ask the patient to look to the left, the right eye fails to adduct and when the patient looks to the right, the left eye fails to adduct. However, both eyes in the patient can adduct during convergence. There is no noticeable strabismus when the eyes are focused on a far point. During abduction, both eyes display nystagmus. You record on the patient's chart a diagnosis of bilateral internuclear opthalmoplegia.
Which of the following neural structures is affected?

A. fourth cranial (trochlear) nerve
B. medial longitudinal fasciculus (MLF)
C. second cranial (optic) nerve
D. sixth cranial (abducens) nerve
E. third cranial (oculomotor) nerve

Correct Answer: B
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
Conjugate movement of the eyes depends on the integrity of the MLF, which links the ipsilateral lateral gaze center in the pons with the contralateral oculomotor nucleus in the midbrain. Lesion of the MLF disconnects these brain nuclei resulting in internuclear ophthalmoplegia and the bilateral condition can be seen in patients with multiple sclerosis. A patient with a lesion of the fourth cranial nerve (choice A) cannot look downward and inward; there is a slight convergent

strabismus when the patient attempts to do so. Lesion of the second cranial nerve (choice C) will result in blindness. Weakness of eye abduction characterizes lesion of the sixth cranial nerve (choice D), which also displays s a convergent strabismus. In a patient with a third cranial nerve (choice E) lesion, the eye is deviated downward and outward (divergent strabismus); ptosis would also be noticeable.

QUESTION 37
You are examining a 12-year-old male patient who has a slowly enlarging, painless swelling in the left inferior region of the neck. After careful palpation and consideration of the results of the radioimaging studies, you diagnose a branchial cyst in the left inferior parathyroid gland. This gland arose in development from which of the following pharyngeal pouches?

A. fifth
B. first
C. fourth
D. second
E. third

Correct Answer: E
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The inferior parathyroid glands and the thymus arise from the third pharyngeal pouch. The superior parathyroid glands develop from the fourth pharyngeal pouch (choice C). The fifth pharyngeal pouch (choice A) in the human is rudimentary or absent. The first pharyngeal pouch (choice B) gives rise to the tympanic membrane, tympanic cavity, mastoid antrum, and pharyngotympanic tube. The palatine tonsil along with the tonsillar sinus and crypts develop from the second pharyngeal pouch (choice D).

QUESTION 38
Regarding the axon of the second-order neuron in the pathway for conscious awareness of fine, discriminative touch and vibratory sensation from the upper limb, which of the following is correct?

A. ascends the brainstem in the medial lemniscus
B. decussates in the ventral white commissure of the spinal cord
C. has its cell body in the nucleus gracilis
D. is found in the dorsal funiculus of the spinal cord
E. terminates in the nucleus cuneatus

Correct Answer: A
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The sensations of discriminative touch and vibration are transmitted through the medial lemniscus. Pain and temperature pathways decussate in the ventral white commisssure (choice B). The nucleus gracilis (choice C) contains neurons that process sensory signals from the lower extremity. The second-order fibers carrying discriminative touch and vibration from the upper limb originate from neurons in the nucleus cuneatus (choice E). First order fibers are found in the dorsal funiculus (choice D).

QUESTION 39
A 60-year-old male patient is brought to the hospital following sudden onset of weakness and sensory loss in the right face and upper limb. The right lower limb is unaffected. An MRI scan would reveal signs of a stroke in which of the following areas?

A. in the territory of the left anterior cerebral artery
B. in the territory of the left middle cerebral artery
C. in the territory of the left posterior cerebral artery
D. in the territory of the right middle cerebral artery
E. in the territory of the right posterior cerebral artery

Correct Answer: B
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
Because the right side of the patient is affected, the stroke is in the territory of the left middle cerebral artery. This artery supplies the lateral aspect of the cerebral hemisphere, including portions of the pre- and postcentral gyri corresponding to the head, upper limb, and trunk on the primary motor (area 4 of Brodmann) and primary sensory (area 3,1,2 of Brodmann) cortical strips. These cortical control areas for the right lower limb are supplied by branches of the left anterior cerebral rtery (choice A), which is uninvolved in this case since the lower limb is intact. The left posterior cerebral artery (choice C) supplies the occipital and temporal lobes and is unaffected in this case. Since the right side of the brain controls the left side of the body and the patient is intact on the left side, none of the right side cerebral arteries (choices D and E) are involved.

QUESTION 40
An 18-year-old male patient was thrown from a horse and suffered extensive damage to the back and pelvic region. After 2 weeks of recovery, it is noted that the patient has a spastic neurogenic urinary bladder. Although the patient is unable to initiate micturition, the bladder periodically empties itself. Where is the lesion affecting control of the bladder in this patient located?

A. cauda equine
B. spinal cord, above the level of S2
C. spinal cord, at the level of S2
D. spinal cord, at the level of S3

E. spinal cord, at the level of S4

Correct Answer: B
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
Since the patient presents with a spastic neurogenic bladder, the lesion is in the spinal cord above the level of S2. The micturition reflex works as follows: when the bladder becomes distended, sensory impulses travel back from the bladder to synapse onto preganglionic parasympathetic neurons located at the levels of S2-S4. These neurons, in turn, excite postganglionic parasympathetic neurons which innervate and cause contraction of the detrusor muscle of the urinary bladder, thus emptying the bladder. This primitive reflex loop comes under supraspinal influence in early childhood when the child learns control of the micturition reflex. When the supraspinal influence is removed, as happens with spinal lesions above the level of S2, the primitive reflex loop remains and the neurogenic spastic bladder empties itself reflexively whenever it becomes full. Lesions in the cauda equina (choice A), or in the spinal cord at the level of S2 (choice B), S3 (choice D), or S4 (choice E) will result in a flaccid bladder because of loss of innervation to the detrusor muscle. In this case, the bladder does not contract by itself and the patient will have to be catherized to prevent cystitis.

QUESTION 41
Papez circuit provides the anatomic substrate for the integration of cognitive, emotional, and expressive brain activities. Which of the following brain structures participates in Papez circuit?

A. amygdale
B. caudate nucleus
C. mammilary nuclei
D. suprachiasmatic nucleus
E. ventrolateral thalamic nucleus

Correct Answer: C
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
Papez circuit is formed by efferent fibers of the hippocampus, which project by way of the fornix to the mammillary nuclei in the hypothalamus. Axons from the mammillary nuclei project to the anterior thalamic nucleus, which is connected to the cingulate gyrus. The latter projects back to the hippocampus by way of the parahippocampal gyrus. Papez circuit integrates cortical, hypothalamic, and thalamic functions resulting in the integration of cognitive, emotional, and expressive brain functions. The ventrolateral thalamic nucleus (choice E) is involved in motor pathways, being connected to the deep cerebellar nuclei and the motor cortex. The caudate nucleus (choice B) is a component of the basal ganglia and the extrapyramidal motor control system. Although the amygdala (choice A) is involved in emotional brain functions, it is not part of Papez circuit. The suprachiasmatic nucleus (choice D) is located in the hypothalamus and mediates the circadian rhythm.

QUESTION 42
Aurologist is teaching her resident to perform a vasectomy. She explains that he has to inject the anesthetic in the skin of the scrotum, in preparation for incision of its lateral aspect. This surgical location allows for easy access to the spermatic cord. Which of the following nerves innervates the skin of the scrotum?

A. femoral nerve
B. iliohypogastric nerve
C. ilioinguinal nerve
D. obturator nerve
E. subcostal nerve

Correct Answer: C
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The anterior aspect of the scrotum is innervated by branches of the ilioinguinal nerve (L1).Other nerves innervating the scrotum are branches of the genitofemoral nerve (L1, L2), pudendal nerve (S2-S4), and posterior femoral cutaneous nerve (S2, S3). The femoral nerve (L2-L4, choice A) supplies sensory innervations to the anteromedial thigh, hip joint, and knee joint. It also innervates muscles of the anterior compartment of the thigh. The iliohypograstric nerve (L1, choice B) provides sensory innervations over the iliac crest and the hypogastric region. The obturator nerve (L2-L4, choice D) supplies motor innervation to the medial compartment of the thigh. The subcostal nerve (T12, choice E) provides motor innervation for the lower part of the external oblique muscle and sensory innervations over the hip and anterior superior iliac spine.

QUESTION 43
Infiltrating or invasive ductal cancer is the most common breast cancer histological type, comprising 7080% of all cases. Invasive breast cancers usually are epithelial tumors of ductal or lobular origin. Which of the following epithelia line the lactiferous ducts?

A. pseudostratified
B. simple squamous
C. stratified cuboidal
D. stratified squamous
E. transitional

Correct Answer: C
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:

The lactiferous duct is lined by a two-cell layered cuboidal epithelium. All other epithelial choices are not found in the breast tissue and are thus incorrect.

QUESTION 44
The abdominal aorta provides for the major blood supply in this region and its branches are organized into paired or unpaired and visceral or parietal branches. Which of the following are paired visceral branches of the abdominal aorta?

A. celiac trunk
B. gonadal arteries
C. inferior phrenic arteries
D. lumbar arteries
E. superior mesenteric artery

Correct Answer: B
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The gonadal arteries are paired visceral branches of the abdominal aorta. Other branches in this category are the suprarenal and renal arteries. The celiac trunk (choice A) and superior mesenteric artery (choice E) are unpaired visceral branches. The inferior phrenic (choice C) and lumbar (choice D) arteries are paired parietal branches.

QUESTION 45
A female patient is diagnosed by sonogram with uterus didelphys (double uterus). The imaging study reveals a bicornuate uterus with a single vagina. During development, the uterus develops from which of the following?

A. mesonephric ducts
B. nephrogenic ridge
C. paramesonephric ducts
D. urogenital sinus
E. yolk sac

Correct Answer: C
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
During development, the uterus develops from fusion of the caudal ends of the para-mesonephric ducts. Failure of fusion results in uterus didelphys. The

mesonephric ducts (choice A) give rise to the epididymis, vas deferens, and ejaculatory duct in the male. The nephrogenic ridge (choice B) is the derivative of the urogenital ridge which will give rise to the urinary system. The urogenital sinus (choice D) gives rise to the urinary bladder, urethra, vagina, and associated glands in the female. The yolk sac (choice E) plays a role in transfer of nutrients before uteroplacental circulation is established, in blood development before the liver begins its hemopoietic activity, and is the site of formation of primordial germ cells.

QUESTION 46
Anewborn infant suffers from a posterolateral defect on the left side of the body. His abdominal contents have herniated through the defect into the thoracic cavity, and as a result, the infant suffers from pulmonary hypoplasia. His breathing difficulty is life threatening because the herniation has inhibited lung development and inflation. This congenital defect is due to a malformation of which of the following?

A. mesentery of the esophagus
B. muscular ingrowth of the body wall
C. pleuropericardial membrane
D. pleuroperitoneal membrane
E. septum transversum

Correct Answer: D
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
congenital defect of the pleuroperitoneal membrane results in an abnormal opening in the posterolateral aspects of the diaphragm. This defect occurs more often on the left side of the body. It is due to the failure of the pleuroperitoneal membrane to form properly and/or to fuse with the other parts of the diaphragm: the mesentery of the esophagus (choice A), the muscular ingrowth of the body wall (choice B), and the septum transversum (choice E). The pleuropericardial membranes (choice C) participate in the formation of the mediastinum and do not contribute to the formation of the diaphragm.

QUESTION 47
A 17-year-old male college student is brought to the emergency room, displaying vomiting, fever, and diarrhea. The patient reports that for a period of 24 hours prior to admission, he suffered from abdominal pain first centered around the navel and then moving inferiorly to the right. As the patient talks, you realize that he is gesturing toward McBurney's point. You tentatively diagnose acute appendicits and request emergency surgery. Accurate visual identification of the appendix during surgery can be verified by using which of the following landmarks?

A. bifurcation of the abdominal aorta
B. epiploic appendages
C. haustra
D. inferior border of the right kidney
E. taeniae coli

Correct Answer: E
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The position of the appendix varies depending on the patient. The taeniae coli are three longitudinal bands of smooth muscle running the length of the colon. Since the appendix is part of the colon, the taeniae coli can be accurately followed to this structure. The bifurcation of the abdominal aorta (choiceA) and inferior border of the right kidney (choice D) are retroperitoneal and would not be of value in identification of the appendix. The epiploic appendages (choice B) are small pockets of fatty tissue along the length of the colon, but they are not found on the appendix. The haustra (choice C) are sacculations of the large intestine resulting from contractions of the taeniae coli.

QUESTION 48
The efferent limb of the pupillary light reflex is interrupted along with corticospinal and orticobulbar fibers in which of the following clinical entities?

A. Broca's aphasia
B. inferior alternating hemiplegia
C. middle alternating hemiplegia
D. superior alternating hemiplegia
E. Wallenberg syndrome

Correct Answer: D
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
Compression of cranial nerve III, in combination with descending corticospinal and corticobulbar fibers, occurs as part of superior alternating hemiplegia. Patients with Broca's aphasia (choice A) typically do not exhibit involvement of the pupillary light reflexes. Inferior alternating hemiplegia (choice B) and middle alternating hemiplegia (choice C) involve cranial nerves XII and VI, respectively, in combination with corticospinal fibers. Wallenberg syndrome (lateral medullary syndrome) (choice E) typically does not include damage to the corticospinal tract.

QUESTION 49
Horner syndrome is sometimes seen in patients diagnosed with the lateral medullary syndrome. Which of the following is a characteristic feature of Horner syndrome?

A. atrophy of tongue musculature
B. mydriasis
C. paralysis of muscles of facial expression
D. profuse sweating
E. red blushing of the skin in the affected area

Correct Answer: E
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The skin in the affected area is red and dry (not moist as in choice D) due to diminished sympathetic activity. The pupil on the affected side is constricted (myosis) (not dilated as in choice B) due to unopposed activity of the sphincter pupillae muscle. Motor deficits such as atrophy of tongue musculature (choice A) or paralysis of facial expression muscles (choice C) are typically not part of Horner syndrome.

QUESTION 50
A 52-year-old male patient with a history of alcoholism is brought to the emergency room because of a sudden onset of right upper quadrant pain, nausea, blood in the vomitus, and fever. Ultrasound diagnosis reveals a portal vein obstruction caused by liver cirrhosis and accompanied by esophageal varices. Proper portal circulation must be reestablished to alleviate the esophargeal varices, and the attending surgeon decides on an end-to-side portocaval shunt. Which of the following describes the chosen procedure?

A. anastomosis by communication between the portal vein and the inferior vena cava
B. anastomosis by prosthetic vascular graft between the inferior vena cava and the superior mesenteric vein
C. anastomosis by suturing the inferior end of the portal vein to the inferior vena cava
D. anastomosis of the splenic vein to the left renal vein
E. placement of an expandable stent between a hepatic vein and the portal vein

Correct Answer: C
Section: Anatomy

Explanation

Explanation/Reference:
Explanation:
Suturing the inferior end of the portal vein to the inferior vena cava is termed end-to-side portocaval shunt, whereas establishing a communication between the portal vein and the inferior vena cava (choice A) is a side-to-side portocaval shunt. Placing a prosthetic vascular graft between the inferior vena cava and the superior mesenteric vein (choice B) is termed a mesocaval shunt. Anastomosis of the splenic vein to the left renal vein (choice D) is a splenorenal or Warren shunt. Placement of an expandable stent between the hepatic vein and portal vein (choice E) is called a transjugular intrahepatic portosystemic shunt or TIPS.

QUESTION 51
During surgical resection of the gastrointestinal tract for treatment of long-standing irritable bowel syndrome, a surgery resident is asked to select a surgical site coinciding with the termination of the vagal innervation. Which of the following does she select?

A. duodenojejunal junction
B. ileocolic junction
C. junction of the second part and third part of the duodenum
D. left colic (splenic) flexure
E. right colic (hepatic) flexure

Correct Answer: D
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The left colic (splenic) flexure represents the junction of the midgut to the hindgut during embryonic development. The vagus (tenth cranial) nerve provides the parasympathetic innervation of the digestive tract up to this flexure, whereas the pelvic parasympathetic fibers from S2-S4 innervate the rest of the tract. The duodenaljejunal junction (choice A), ileocolic junction (choice B), and rightcolic (hepatic) flexure (choice E) are anatomical landmarks along the digestive tract without change in parasympathetic innervation. The junction of the second part and third part of the duodenum (choice C) represents the embryonic junction between the foregut and the midgut, but both receive vagal innervation.

QUESTION 52
The structure indicated by arrow 1 in following figure is innervated by which of the following?

A. anterior ethmoidal nerve
B. greater palatine nerve
C. lesser palatine nerve
D. middle superior alveolar nerve
E. nasopalatine nerve

Correct Answer: D
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
Arrow 1 points to the maxillary sinus, which is innervated by the posterior, middle, and anterior superior alveolar nerves. The latter are branches from the infraorbital nerve arising from the maxillary division (V2) of the trigeminal (fifth cranial) nerve. The anterior ethmoidal nerve (choice A) is a branch of the nasociliary nerve from the ophthalmic division (V1) of the trigeminal nerve. The greater palatine nerve (choice B) and lesser palatine nerve (choice C) are branches of the maxillary division of the trigeminal nerve supplying the hard and soft palate, respectively. The nasopalatine nerve (choice E) is derived from the maxillary division of the trigeminal nerve and supplies the nasal septum.

QUESTION 53
Which of the following thalamic nuclei subserves a motor function?

A. dorsomedial nucleus
B. lateral geniculate nucleus
C. medical geniculate nucleus
D. ventral lateral nucleus
E. ventral posterior medial nucleus

Correct Answer: D
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The ventral lateral nucleus of the thalamus receives projections from the deep cerebellar nuclei and, in turn, sends projections to the motor cortex. It is thus functionally defined as a thalamic motor nucleus. The dorsomedial nucleus (choice A) is considered a limbic nucleus of the thalamus as it receives projections from the amygdala and olfactory cortex, and projects to the prefrontal cortex and hypothalamus. The lateral (choice B) and medial geniculate (choice C) nuclei and the ventral posterior medial nucleus (choice D) are considered sensory nuclei as they receive information mediating vision, audition, and somatosensory signals from the face, respectively. In turn, these three brain areas project to the somatosensory cortex.

QUESTION 54
A neurology resident is testing the jaw-jerk reflex in a patient by tapping gently on the right masseter muscle and observing elevation of the mandible. What is the location of the neuronal cell bodies of the proprioceptive fibers mediating the jaw-jerk reflex?

A. mesencephalic trigeminal nucleus
B. motor trigeminal nucleus

C. principal (main) trigeminal nucleus
D. spinal trigeminal nucleus
E. trigeminal (gasserian) ganglion

Correct Answer: A
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The jaw-jerk reflex is a monosynaptic (stretch) reflex for the masseter muscle. Proprioceptive fibers from the muscle travel by way of the trigeminal nerve back to their cell bodies in he mesencephalic trigeminal nucleus. Projections from this nucleus synapse on motor neurons of the motor trigeminal nucleus (choice B) which elicits contraction of the masseter muscle. The principal (main) trigeminal nucleus (choice C) receives light touch sensory information from the face, whereas the spinal trigeminal nucleus (choice D) receives pain and temperature sensations. The trigeminal (gasserian) ganglion (choice E) contains the cell bodies of all sensory neurons projecting to the principal (main) and spinal trigeminal nuclei.

QUESTION 55
Which of the following statements concerning muscle spindles is correct?

A. Activation of type Ia sensory fibers from a given spindle leads to inhibition of the muscle in which that spindle is located.
B. Alpha motoneurons synapse directly with intrafusal muscle fibers.
C. Each intrafusal fiber is innervated by two different gamma motoneurons.
D. Only one type of intrafusal muscle fiber (cell) is present in most muscle spindles.
E. Type Ia sensory fibers from a spindle form direct synaptic contact with alpha motoneurons in the spinal cord.

Correct Answer: E
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The type Ia sensory fibers from a spindle form direct excitatory synapses with alpha motoneurons. Activation of type Ia sensory fibers (choice A) leads to excitation of the muscle in which that spindle is located. Alpha motoneurons (choice B) synapse with extrafusal muscle fibers, whereas gamma motoneurons synapse with intrafusal muscle fibers. Each intrafusal muscle fiber (choice C) is innervated by only one gamma motoneuron. Each muscle spindle contains a mixture of both nuclear bag and nuclear chain intrafusal fibers, not just one type as indicated in choice D.

QUESTION 56
Which of the following is characteristic of damage to the corticospinal (pyramidal) system?

A. Babinski's sign
B. flaccid paralysis and hypotonia
C. immediate muscle degeneration and atrophy
D. intention tremor
E. loss of deep tendon reflexes

Correct Answer: A
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The Babinski sign--dorsiflexion of the great toe in response to stroking the plantar aspect of the foot-- is a characteristic sign of pyramidal tract involvement. Signs and symptoms of corticospinal tract injury that are nearly always apparent to some degree include spastic paralysis, hypertonia, loss of deep tendon reflexes, and hyperactive abdominal and cremasteric reflexes. Flaccid paralysis and hypotonia (choice B) are commonly seen following lower motoneuron injury, as is loss of deep tendon reflexes (choice E). Muscle degeneration and atrophy (choice C) are not characteristic symptoms of corticospinal tract damage. The presence of an intention tremor (choice D) is a sign of cerebellar damage, and is not seen with corticospinal tract lesions.

QUESTION 57
Cilia are anchored to the apical portion of certain types of epithelial cells and they are mobile. Which of the following form the motile cytoskeletal component of the cilia?

A. intermediate filaments
B. microfilament
C. microtubule
D. neurofilament
E. tonofilaments

Correct Answer: C
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
Acilium is formed by a concentric array of nine microtubule doublets surrounding a central pair of microtubules (9 + 2 organization). Intermediate filaments (choice A) are intermediate in diameter size (10 nm) between the microtubules (25 nm) and the microfilaments (7 nm). They do not confer motility to the cilia. They instead participate in the cytoskeletal integrity of nerve cells, neurofilaments (choice D) or hemidesmosomes, tonofilaments (choice E). Microfilaments (choice B) are found in microvilli and stereocilia.

QUESTION 58
A 79-year-old female patient was admitted to the hospital, presenting with fever, vomiting, dehydration, and distension of the abdomen. An X-ray reveals ileus and exploratory surgery reveals occlusion of vasa recta of the jejunum. Which of the following arteries supply branches to the involved vasa recta?

A. ileocolic artery
B. inferior pancreaticoduodenal artery
C. right colic artery
D. right gastroepiploic artery
E. superior mesenteric artery

Correct Answer: E
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
Ileus is obstruction of the intestine, in this case due to paralysis resulting from ischemia. The jejunum receives its vascular supply from jejunal branches arising from the superior mesenteric artery. The ileocolic artery (choice A) supplies the ileum, ileocolic junction, and the appendix. The inferior pancreaticoduodenal artery (choice B) provides vascular innervations to the pancreas and duodenum, and forms the anastomosis between the foregut and midgut. The right colic artery (choice C) supplies the ascending colon and the right gastroepiploic artery (choice D) the greater curvature of the stomach and greater omentum.

QUESTION 59
Which of the following is directly involved with the descending modulation of pain transmission?

A. dopamine
B. MLF
C. nucleus raphe magnus
D. rubrospinal fibers
E. ventral lateral thalamic nucleus

Correct Answer: C
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The nucleus raphe magnus receives input from the periaqueductal gray and gives rise to descending serotonergic fibers of the raphe spinal projection. The latter fibers activate enkephalinergic spinal cord interneurons that presynaptically inhibit incoming pain fibers at their initial synapse in the spinal cord dorsal horn. The neurotransmitter dopamine (choice A) has not been shown to be involved in the descending systems that modulate pain transmission. The MLF (choice B) is an

ascending fiber system in the brainstem that is primarily involved in the control of eye movements. The rubrospinal system (choice D) is a descending fiber tract involved with the control of limb musculature. The ventral lateral nucleus of the thalamus (choice E) is primarily involved with motor function and does not contribute to descending pathways that influence pain transmission.

QUESTION 60
Which of the following vessels participate in the arterial circulation of the spleen?

A. afferent arteriole
B. efferent arteriole
C. interlobar arteries
D. interlobular arteries
E. sheathed arteriole

Correct Answer: E
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The spleen receives its blood supply from the splenic artery, which branches off from the celiac trunk from the abdominal aorta. At the hilum of the spleen, the splenic artery branches off into trabecular arteries, which enter the spleen along the trabeculae and branch in the parenchyma as central arteries running in the white pulp. The central arteries branch into penicillar arterioles, which give rise to capillaries and sheathed arterioles. The capillaries feed the marginal sinuses as well as the red pulp sinuses. Afferent (choice A) and efferent (choice B) arterioles, and interlobar (choice C) and interlobular (choice D) arteries are vessels found in the kidney.

QUESTION 61
A middle-aged, markedly obese male patient presents to the emergency room with pain in the inguinal region. Examination reveals an abnormal bulge which increases in size when the patient performs the Valsava maneuver. The bulge can be reduced manually when the patient is lying supine. However, as soon as the patient stands up and coughs, the bulge reappears. The patient is diagnosed with an inguinal hernia. The chief resident in surgery asks for a determination of whether the hernia is direct or indirect. Which of the following is a useful landmark to distinguish an indirect from a direct inguinal hernia?

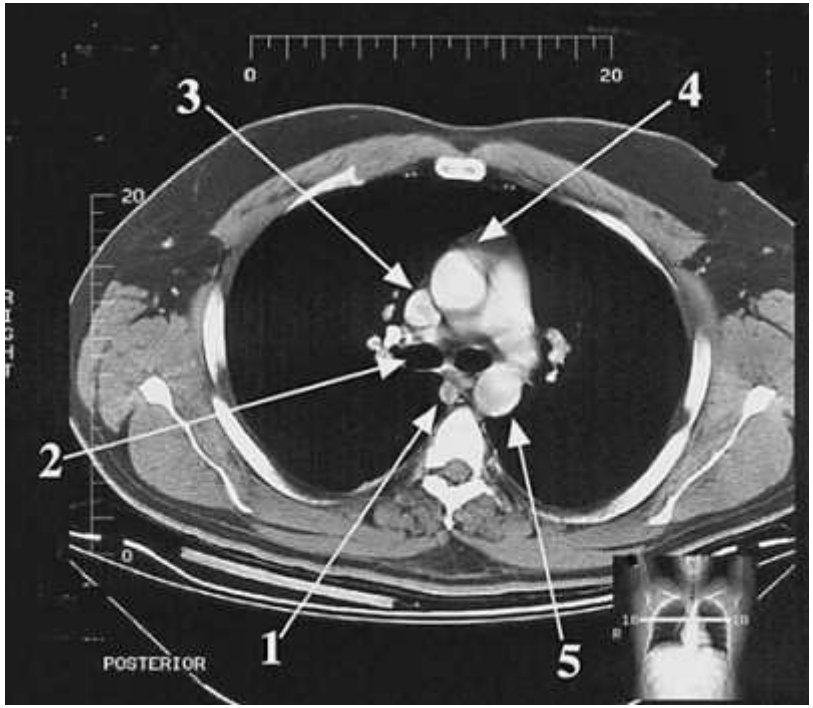
A. anterior superior iliac spine
B. inferior epigastric vessels
C. inguinal ligament
D. pubic tubercle
E. umbilicus

Correct Answer: B
Section: Anatomy

Explanation

Explanation/Reference:
Explanation:
The inferior epigastric vessels lie medial to the deep inguinal ring. An indirect inguinal hernia leaves the abdominal cavity through the deep inguinal ring and is thus always localized lateral to the inferior epigastric vessels. Adirect inguinal hernia results from weakness in the posterior wall of the inguinal canal and pushes through the conjoint tendon to reach the superficial inguinal ring. The direct inguinal hernia is thus always located medial to the inferior epigastric vessels. The anterior superior iliac spine (choice A) and pubic tubercle (choice D) are respectively located too far laterally or medially to be of use in distinguishing indirect from direct hernias. The inguinal ligament (choice C) is used to istinguish a femoral hernia which is always located inferior to this structure. The umbilicus (choice E) is the site for an umbilical hernia and not inguinal hernias.

QUESTION 62
A fourth-year medical student is learning to place a central line. To prepare for this procedure, she reviews X-rays and CT scans in order to gain a proper three-dimensional relationship of the structures involved. In following figure what is the structure pointed to by arrow 1?



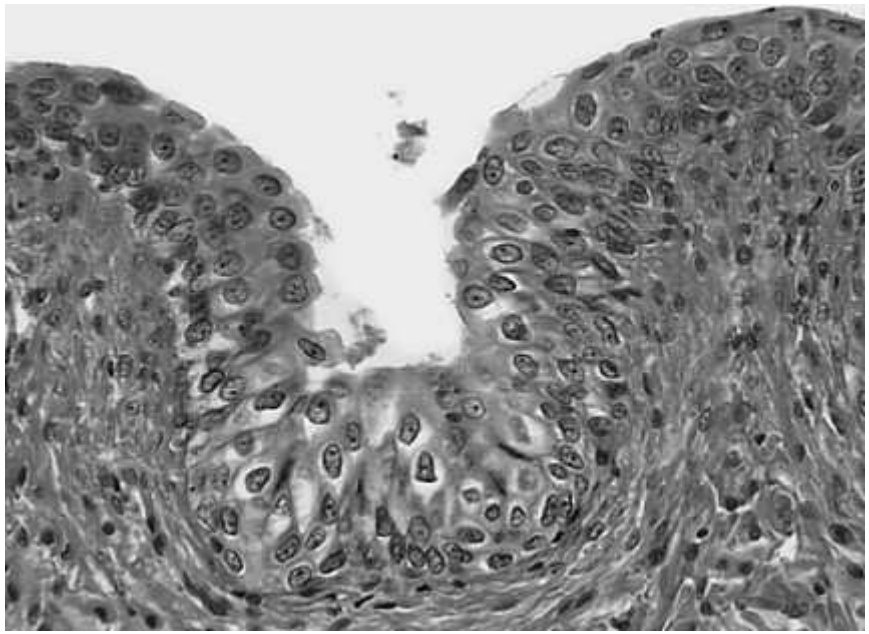
A. Ascending aorta
B. Azygos vein

C. Descending aorta
D. Right bronchus
E. Superior vena cava

Correct Answer: E
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
Arrow 1 points to the superior vena cava. The central venous catheter is inserted into the subclavian vein and threaded into the superior vena cava. The ascending aorta (choice A) is labeled by arrow 4 and its counterpart, the descending aorta (choice C) by arrow 5. The azygos vein (choice B) is indicated by arrow 1. Arrow 2 indicates the right bronchus (choice D) just as it leaves the carina.

QUESTION 63
Referring to following figure what is the most likely source of this epithelium?



A. gall bladder

B. salivary duct
C. thick skin
D. trachea
E. urinary bladder

Correct Answer: E
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The appearance of this epithelium reveals it to be transitional epithelium. It is stratified with a scalloped surface outline. The cells at the bottom layer are cuboidal in appearance and stained darkly; cells in the intermediate layer are polygonal. Cells at the surface of the epithelium are pale-stained, rounded, and large. Transitional epithelium is characteristic of organs of the urinary system, such as the urinary bladder. The gall bladder (choice A) is characterized by simple columnar epithelium. The epithelium of the salivary gland (choice B) is simple cuboidal epithelium. Thick skin (choice C) is made up of stratified squamous epithelium and the trachea (choice D) is lined with pseudostratified columnar epithelium.

QUESTION 64
Afailure of the truncoconal septum to follow a spiral course results in which of the following conditions?

A. common atrium
B. persistent atrioventricular canal
C. persistent truncus arteriosus
D. Tetralogy of Fallot
E. transposition of the great vessels

Correct Answer: E
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
Transposition of the great vessels occurs when the truncoconal ridges fail to spiral as they divide the outflow tract into two channels. This produces two totally independent circulatory loops with the right ventricle feeding into the aorta and the left ventricle feeding into the pulmonary artery. Common atrium (choice A) results from a complete failure of the septum primum and septum secundum to form. Persistent atrioventricular canal (choice B) results from a failure of the endocardial cushions to fuse and partition the atrioventricular canal into a right and left component. It is accompanied by defects of the atrial and ventricular septa. Persistent truncus arteriosus (choice C) results from a total failure of the truncoconal ridges to develop and partition the outflow tract of the developing heart. Tetralogy of Fallot (choice D) is a related group of defects with the primary malformation being an unequal division of the outflow tract, resulting in pulmonary stenosis. The other eatures of tetralogy are an interventricular septal defect, an overriding aorta, and right ventricular hypertrophy. Survival of the infant depends on the maintenance of a patent ductus arteriosus.

QUESTION 65
During surgery to repair a strangulated inguinal hernia, it is discovered that the left testicular vein is thrombosed and must be repaired. The left testicular vein normally drains into which of the following?

A. inferior vena cava
B. left renal vein
C. right common iliac vein
D. right femoral vein
E. right renal vein

Correct Answer: B
Section: Anatomy
Explanation

Explanation/Reference:
The left testicular vein drains into the left renal vein. The inferior vena cava (choice A) receives the right testicular vein. The equivalent relationship holds true in the female where the left ovarian vein drains into the left renal vein and the right ovarian vein into the inferior vena cava. The right common iliac vein (choice C), right femoral vein (choice D), and right renal vein (choice E) do not receive gonadal veins.

QUESTION 66
The sensory innervation of the posterior onethird of the tongue is performed by cranial nerve IX (glossopharyngeal). During development, this region of the tongue develops from which of the following pharyngeal arches?

A. first
B. fourth
C. second
D. sixth
E. third

Correct Answer: E
Section: Anatomy
Explanation

Explanation/Reference:
The posterior one-third of the tongue is derived from the third pharyngeal arch and is thus innervated by cranial nerve IX (glossopharyngeal). The first pharyngeal arch (choice A) and second pharyngeal arch (choice C) give rise to the anterior two-thirds of the tongue. The mandibular division of cranial nerve V (trigeminal) provides general sensation to the anterior two-thirds of the tongue, and cranial nerve VII via the chorda tympani provides special sensation (taste). The fourth pharyngeal arch (choice B) gives rise to the epiglottis and, along with the sixth pharyngeal arch (choice D), to the laryngeal cartilages. The nerve to the fourth

pharyngeal arch is cranial nerve X (vagus).

QUESTION 67
The sinoatrial (SA) node initiates the heartbeat by giving off an impulse about 80 times per minute. It is located at the junction of the superior vena cava and right atrium. In about 60% of the cases, the SA node derives its vascular supply from which of the following?

A. anterior interventricular artery
B. left circumflex artery
C. posterior interventricular artery
D. right coronary artery
E. right marginal branch

Correct Answer: D
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
In 60% of patients, the right coronary artery supplies the SA node. In a third of the population, the SA node is supplied by the left coronary artery and in some patients it receives branches from both the right and the left. The anterior interventricular (choice A) and left circumflex (choice B) arteries are distal branches of the left coronary artery, too distant to supply the SA node. The right coronary artery normally gives out its SA nodal branch in its proximal portion and then distally gives rise to the right marginal (choice E) and posterior interventricular (choice C) arteries. These are also too distant to supply the SA node.

QUESTION 68
In elderly patients (over 60 years of age), fractures of the neck of the femur following a fall are common. Arterial branches supplying the femoral head and neck are vulnerable to injury during these fractures, and the resulting posttraumatic avascular necrosis affects the head of the femur. In the adult, the most important direct vascular source to the femoral head and neck is which of the following?

A. artery to the head of the femur
B. femoral artery
C. lateral circumflex femoral artery
D. medial circumflex femoral artery
E. superior gluteal artery

Correct Answer: D
Section: Anatomy
Explanation

Explanation/Reference:

Explanation:
The medial circumflex femoral artery supplies the most important source of blood to the femoral head and neck. This artery anastomoses with the artery to the head of the femur (choice A), which arises from the obturator artery. However, if the medial circumflex femoral artery is injured, the blood flow in the small artery to the head of the femur may not be sufficient to prevent posttraumatic avascular necrosis of the femoral head. Normally, the medial and lateral circumflex femoral arteries arise from the deep artery of the thigh, but occasionally they arise from the femoral artery (choice B). However, the femoral artery is not a direct vascular source to the head of the femur. The lateral circumflex femoral artery (choice C) and superior gluteal artery (choice E) also supply the hip joint, but their contribution to the head and neck of the femur is less than that of the medial femoral circumflex artery.

QUESTION 69
A 38-year-old female patient suffers from pleurisy and requires pleural fluid sampling (thoracentesis). The attending physician asks you to perform the procedure at the midaxillary line on the right side. Which of the following would be the appropriate level to perform the procedure?

A. above the level of the 7th rib
B. at the level of the 10th rib
C. at the level of the 5th rib
D. below the level of the 10th rib
E. between the level of the 8th and 10th ribs

Correct Answer: E
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The needle for thoracentesis should be inserted in the intercostals spaces between the 8th and 10th ribs. Remember that the parietal pleura extends approximately two ribs inferior to the lung: at the midaxillary line, the inferior surface at the lung is at the level of the 8th rib and the parietal pleura at the 10th rib. Above the level of the 7th (choice A) and 5th (choice C) ribs, the needle will injure the lung. At (choice B) or below the level of the 10th rib (choice D), it will injure the liver or other abdominal organs.

QUESTION 70
A 45-year-old female patient develops Parinauds syndrome (vertical gaze palsy) and an MRI shows a large tumor of her pineal gland. The tumor is not only compressing her tectum, causing the vertical gaze palsy, but also obstructing the underlying cerebrospinal fluid pathway causing progressive noncommunicating hydrocephalus. The obstruction causes immediate accumulation of cerebrospinal fluid in which of the following?

A. cerebral aqueduct of Sylvius
B. fourth ventricle
C. lateral ventricle
D. subarachnoid space
E. third ventricle

Correct Answer: E
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
In this situation, the cerebrospinal fluid will accumulate immediately in the third ventricle and cause hydrocephalus. The flow of cerebrospinal fluid is normally from the lateral ventricles (choice C) to the third ventricle and then by way of the cerebral aqueduct of Sylvius (choice A) to the fourth ventricle (choice B). From there the cerebrospinal fluid flows out of the brain into the subarachnoid space (choice D). A blockage of the cerebral aqueduct will result in immediate accumulation of cerebrospinal fluid in the third ventricle. Because the cerebrospinal fluid no longer flows from the ventricular system to the subarachnoid space, the resulting hydrocephalus is termed noncommunicating.

QUESTION 71
Apatient has been severely injured in the back of the head during a mugging attempt and imaging studies reveal possible fracture of the skull along with the C1 (atlas) vertebra. The patient is also hemorrhaging from the vertebral artery in this location, and the attending surgeon will attempt to stop the bleeding by access through the suboccipital triangle. Which of the following muscles attaches from the transverse process of C1 to the occipital bone and forms the lateral border of the suboccipital triangle?

A. obliquus capitis inferior
B. obliquus capitis superior
C. rectus capitis posterior major
D. rectus capitis posterior minor
E. semispinalis cervicis

Correct Answer: B
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The obliquus capitis superior, attached between the transverse process of C1 and the suboccipital bone between the nuchal lines. It forms the lateral border of the suboccipital triangle. The obliquus capitis inferior (choice A) is the inferior border of the triangle, attaching from the spinous process of C2 to the transverse process of C1. The rectus capitis posterior major (choice C) inserts from the spinous process of C2 into the inferior nuchal line on the occipital bone; it forms the medial border of the suboccipital triangle. The rectus capitis posterior minor (choice D) lies medial to the rectus capitis posterior major. The semispinalis cervicis (choice E) does not participate in the formation of the suboccipital triangle.

QUESTION 72
Your patient presents in your office complaining of hoarseness. During your examination, you find that one vocal fold has deviated toward the midline and does not abduct during deep inspiration or vocalization. You also observe that touch sensation in the vestibule of the larynx appears to be intact. Which laryngeal muscle is most important in abduction of the vocal folds?

A. cricothyroid
B. lateral cricoarytenoid
C. posterior cricoarytenoid
D. thyroarytenoid
E. transverse arytenoid

Correct Answer: C
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The vocal folds are abducted and the rima glottidis is widened by the posterior cricoarytenoid muscles that rotate the arytenoid cartilages laterally. The cricothyroid muscles (choice A) tense and lengthen the vocal ligament by tilting the thyroid cartilage forward. The lateral cricoarytenoid muscles (choice B) adduct the vocal folds by medially rotating the arytenoid cartilages. The thyroarytenoid muscles (choice D) decrease the tension and length of the vocal ligaments by tilting the thyroid cartilages posteriorly. The transverse arytenoids muscle (choice E) adducts the vocal folds by pulling the arytenoid cartilages together.

QUESTION 73
Your patient presents in your office complaining of hoarseness. During your examination, you find that one vocal fold has deviated toward the midline and does not abduct during deep inspiration or vocalization. You also observe that touch sensation in the vestibule of the larynx appears to be intact.

You suspect that a nerve has been damaged, but which nerve is most likely involved?

A. external laryngeal
B. glossopharyngeal
C. inferior laryngeal
D. internal laryngeal
E. superior laryngeal

Correct Answer: C
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The inferior laryngeal nerve is motor to the intrinsic muscles of the larynx except the cricothyroid muscle, and is sensory to the larynx below the level of the vocal fold. The external laryngeal nerve (choice A) is the branch of the superior laryngeal nerve that contains the motor fibers to the cricothyroid muscle and to the cricopharyngeus muscle. The glossopharyngeal nerve (choice B) does not supply either motor or sensory fibers to the larynx. The internal laryngeal nerve (choice

D) is the branch of the superior laryngeal nerve that contains the sensory fibers to the laryngeal mucosa above the vocal fold. The superior laryngeal nerve (choice E) is sensory to the laryngeal mucosa above the vocal fold and also includes motor fibers to the cricothyroid muscle.

QUESTION 74
During maturation of the oocytes, which of the following structures retain almost all of the cytoplasm after the first meiotic division?

A. first polar body
B. ovum
C. primary oocyte
D. second polar body
E. zygote

Correct Answer: B
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The first meiotic division results in two secondary oocytes: the ovum retains almost all of the cytoplasm whereas the first polar body (choice A) does not. Primary oocytes (choice C) are the cells undergoing the first meiotic division. The second polar body (choice D) is formed after the second meiotic division. The zygote (choice E) is the fertilized ovum.

QUESTION 75
Your patient reports that several days earlier he "threw his back out" when he bent from the waist and picked up a very heavy package. The pain was immediate and extended from his hip, down the back of the thigh, and into his leg and foot. As he lies on the examining table, you raise his leg by the foot keeping the knee extended and elicit intense pain over the distribution of the sciatic nerve. An MRI scan confirms your conclusion that your patient has a herniated intervertebral disk between the fourth and fifth lumbar vertebrae.
Intervertebral disks may protrude or rupture in any direction, but they most commonly protrude in which direction?

A. anteriorly
B. anterolaterally
C. laterally
D. posteriorly
E. posterolaterally

Correct Answer: E
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
Intervertebral disks may protrude or rupture in any direction but do so most commonly in a posterolateral direction, just lateral to the strong central portion of the posterior longitudinal ligament. This is usually the weakest part of the disk, because the annulus is thinner here and is not supported by other ligaments. Anteriorly (choice A) the intervertebral disks are supported by the broad and strong anterior ligament. Herniation is less common in this direction. Anterolaterally (choice B) the intervertebral disk is supported by the broad anterior longitudinal ligament. The nucleus pulposus is also situated posteriorly in the disk, making herniation here less likely. Herniation of the intervertebral disk laterally (choice C) is not particularly common. Posteriorly (choice D) the intervertebral disks are supported by the posterior longitudinal ligament. Herniation is less common in this direction.

QUESTION 76
Your patient reports that several days earlier he "threw his back out" when he bent from the waist and picked up a very heavy package. The pain was immediate and extended from his hip, down the back of the thigh, and into his leg and foot. As he lies on the examining table, you raise his leg by the foot keeping the knee extended and elicit intense pain over the distribution of the sciatic nerve. An MRI scan confirms your conclusion that your patient has a herniated intervertebral disk between the fourth and fifth lumbar vertebrae.
Herniation of the intervertebral disk between the fourth and fifth lumbar vertebrae most likely impinges on the roots of which spinal nerve?

A. L3
B. L4
C. L5
D. S1
E. S2

Correct Answer: C
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
A bulging or protruded disk typically affects the traversing nerve root; that is, the nerve affected is one number greater than the number of the disk. The L3 spinal nerve (choice A) would be affected by protrusion of the L2 intervertebral disk. The L4 spinal nerve (choice B) would be affected by protrusion of the L3 intervertebral disk. The S1 spinal nerve (choice D) would be affected by protrusion of the L5 intervertebral disk. The S2 spinal nerve (choice E) exits through the foramina of the fused sacrum and, therefore, is not subject to compression by herniated intervertebral disks.

QUESTION 77
An opera singer, who has maintained a demanding work schedule, worries about the effect on her vocal cords. The epithelium covering the vocal cords is which of the following?

A. pseudostratified ciliated
B. simple columnar
C. simple cuboidal

D. simple squamous
E. stratified squamous

Correct Answer: E
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
A stratified squamous epithelium covers the vocal cords or folds. This epithelium protects the underlying tissue from the mechanical stress acting on the surface of the vocal cords. A simple squamous epithelium (choice D) is not suitable for protection. The rest of the larynx is covered with a pseudostratified ciliated epithelium (ie, a respiratory epithelium [choice A]). Simple columnar (choice B) and simple cuboidal (choice C) epithelia are found more commonly in organs with secretory or absorptive functions.

QUESTION 78
A patient suffers from Frey's syndrome manifested by perspiration of the skin covering the left parotid gland whenever the patient eats. On inquiry, the patient reveals that he suffered deep injuries on that side of his face and neck in an automobile accident. You explain to him that his syndrome results from abnormal connections between the great auricular nerve and parasympathetic secretomotor fibers, which normally innervate only the parotid gland. This abnormal reinnervation occurred during the healing period after the accident. The parasympathetic secretomotor fibers to the parotid gland are carried by which of the following?

A. auriculotemporal nerve
B. buccal branch of the facial nerve
C. buccal nerve
D. greater petrosal nerve
E. lesser petrosal nerve

Correct Answer: A
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The auriculotemporal nerve is a branch of the mandibular division of the trigeminal nerve. It carries postganglionic parasympathetic fibers from the otic ganglion to the parotid gland. The buccal nerve (choice C) is a sensory branch of the mandibular division of the trigeminal nerve. It innervates the gingival adjacent to the two posterior molar teeth, the mucosa, and skin of the cheek. The buccal branch of the facial nerve (choice B) provides motor innervation to the muscles around the mouth. The greater petrosal nerve (choice D) is a branch of the facial nerve from the geniculate ganglion. It carries preganglionic parasympathetic fibers to the pterygopalatine ganglion. The lesser petrosal nerve (choice E) is a continuation of the tympanic branch of the glossopharyngeal nerve and carries preganglionic parasympathetic fibers to the otic ganglion.

QUESTION 79
Your young female patient has a large bulge on the anterior thigh below the inguinal ligament. You suspect an abdominal hernia that has passed through the femoral ring into the femoral sheath and then through the saphenous hiatus into the subcutaneous layer of the upper thigh. In addition to the hernia sac, you would expect the femoral canal to contain which of the following?

A. connective tissue and lymph nodes
B. femoral artery
C. femoral nerve
D. femoral vein
E. great saphenous vein

Correct Answer: A
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The femoral canal, the medial compartment of the femoral sheath, contains only a slight amount of loose connective tissue and one or two lymphatic vessels and nodes. The femoral artery (choice B) is found in the lateral compartment of the femoral sheath with the genital branch of the genitofemoral nerve. The femoral nerve (choice C) is the most lateral structure in the femoral triangle, but it does not lie within the femoral sheath. The femoral vein (choice D) occupies the intermediate compartment of the femoral sheath. The saphenous vein (choice E) is a superficial vein that passes through the saphenous hiatus to end in the femoral vein. It does not lie within the femoral canal.

QUESTION 80
Sensations from the thoracic and abdominal organs are usually difficult to localize. They are conveyed by general visceral afferent (GVA) fibers, which synapse in which of the following nuclei?

A. ambiguus nucleus
B. dorsal motor nucleus of the vagus
C. hypoglossal nucleus
D. solitary nucleus
E. spinal (descending) trigeminal nucleus

Correct Answer: D
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:

GVA fibers from the thoracic and abdominal organs have their perikarya in the inferior vagal (nodose) ganglion and project to the solitary nucleus. The ambiguus nucleus (choice A) provides branchial efferent (motor) fibers to the stylopharyngeus, soft palate, pharyngeal, and laryngeal muscles. The dorsal motor nucleus of the vagus (choice B) sends parasympathetic preganglionic fibers to the thoracic and abdominal viscera. The hypoglossal nucleus (choice C) provides motor innervation for the muscles of the tongue. The spinal (descending) trigeminal nucleus (choice E) receives pain and temperature fibers from the face area.

QUESTION 81
Corneal abrasions produce eye pain and excessive lacrimation. Which cranial nerve innervates the cornea?

A. fifth (trigeminal)
B. fourth (trochlea)
C. second (optic)
D. sixth (abducens)
E. third (oculomotor)

Correct Answer: A
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The ophthalmic division of cranial nerve V (trigeminal) provides general sensory innervations to the eyeball, including the cornea. Cranial nerve II (optic, choice C) carries the visual function of the retina of the eye. Cranial nerves IV (trochlea, choice B) and VI (abducens, choice D) innervate the superior oblique and lateral rectus muscles, respectively. The innervation of all other extraocular muscles is performed by cranial nerve III (oculomotor, choice E).

QUESTION 82
The anterior two-thirds of the tongue differ from the posterior one-third of the tongue by its special visceral afferent (SVA; taste) innervation. The perikarya of neurons providing the sensation of taste in the anterior two-thirds of the tongue are found in which of the following?

A. geniculate ganglion
B. otic ganglion
C. pterygopalatine (sphenopalatine) ganglion
D. submandibular ganglion
E. trigeminal (gasserian) ganglion

Correct Answer: A
Section: Anatomy
Explanation

Explanation/Reference:

Explanation:
SVA (taste) fibers have their perikarya in the geniculate ganglion located in the petrous portion of the temporal bone. These neurons project their axons to the gustatory nucleus in the brainstem. The otic ganglion (choice B) receives preganglionic parasympathetic fibers originating from the inferior salivatory nucleus by way of the ninth cranial (glossopharyngeal) nerve. In turn, it projects postganglionic parasympathetic fibers to the parotid salivary gland. The pterygopalatine (sphenopalatine) ganglion (choice C) is also a parasympathetic ganglion, which receives preganglionic fibers from the superior salivatory nucleus by way of the ninth cranial (glossopharyngeal) nerve. In turn, it sends postganglionic parasympathetic fibers to the lacrimal gland and mucous glands in the nose. The submandibular ganglion (choice D) receives preganglionic parasympathetic fibers from the chorda tympani, a branch of the nervus intermedius which runs with the seventh cranial nerve. It innervates the submandibular and sublingual salivary glands. The trigeminal (gasserian) ganglion (choice E) receives sensations from the face, mucosa, cornea, teeth, gum, palate, and the anterior two- thirds of the tongue. It sends projections to the principal sensory and spinal trigeminal nuclei in the brainstem.

QUESTION 83
You are concerned that your patient may have compromised function of the mitral valve. The sound of the mitral valve is best heard at which of the following locations?

A. at the apex in the left fifth intercostals space in the midclavicular line
B. at the xiphisternal junction
C. in the fifth intercostal space to the right of the sternum
D. in the second intercostal space to the left of the sternum
E. in the second intercostal space to the right of the sternum

Correct Answer: A
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
There is only one point of the heart that can be directly identified on the precordium: the apex. A cardiac impulse may be visible at the apex, and palpation over it confirms the presence of the apex beat. The apex is located in the left fifth intercostal space just medial to the midclavicular line, and is the point where the mitral valve is best heard. None of the heart sounds are best heard at the xiphisternal junction (choice B). The tricuspid valve is best heard in the fifth intercostal space to the right of the sternum (choice C). The pulmonary valve is best heard in the second intercostal space to the left of the sternum (choice D). The aortic valve is best heard in the second intercostals space to the right of the sternum (choice E).

QUESTION 84
A 14-year-old female patient complains of a severe sore throat and you use a cotton swab to obtain specimens for a culture. As you lightly touch the pharyngeal wall with the cotton swab, the patient gags. What is the location of neuronal cell bodies innervating pharyngeal constrictor muscles involved in the gag reflex?

A. abducens nucleus
B. ambiguus nucleus
C. dorsal motor nucleus of the vagus

D. facial nucleus
E. hypoglossal nucleus

Correct Answer: B
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
Motor innervation of the pharyngeal constrictor muscles is derived from the ambiguous nucleus in the medulla oblongata. These motor fibers reach the constrictor muscles via the vagus nerve. The abducens nucleus (choice A) provides motor innervation to the lateral rectus muscle of the eye. The dorsal motor nucleus of the vagus (choice C) provides preganglionic parasympathetic innervation for the organs of the thorax and abdomen. The facial nucleus (choice D) sends motor innervation to the muscles of facial expression and the stapedius. The hypoglossal nucleus (choice E) innervates the muscles of the tongue.

QUESTION 85
A newborn infant displays wheezing respiration, which is aggravated when she feeds, flexes her neck, and/or cries. Radioimaging studies of her chest reveal a double aortic arch compressing her trachea and esophagus. This rare developmental defect results from persistence of the right dorsal aorta, which normally disappears. The arch of the aorta arises from which of the following structures?

A. fifth pair of aortic arches
B. fourth pair of aortic arches
C. second pair of aortic arches
D. sixth pair of aortic arches
E. third pair of aortic arches

Correct Answer: B
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The arch of the aorta is formed from the left fourth aortic arch. Part of the right fourth aortic arch becomes the proximal portion of the right subclavian artery, whereas the rest of the fourth arch disappears. However, if it persists, a right aortic arch is formed passing posterior to the trachea and esophagus. With the formation of the normally occurring left aortic arch, which runs anterior to the trachea and esophagus, a double aortic arch is created. This defect clamps the trachea and esophagus resulting in the respiratory symptoms. The second pair of aortic arches (choice C) partially form the stapedial arteries in the middle ear of the embryo. The third pair of aortic arches (choice E) form the common carotid arteries and contribute to the internal carotid arteries. The fifth pair of aortic arches (choice A) either does not develop or form primitive vessels, which disappear eventually. The sixth pair of aortic arches (choice D) contribute to the formation of the pulmonary arteries and ductus arteriosus.

QUESTION 86

After recovery from the surgical removal of the thyroid gland, the quality of the voice in a patient changed to a monotone. It was discovered that the cricothyroid muscle in this patient was paralyzed. The cricothyroid muscle is innervated by which of the following?

A. accessory nerve
B. ansa cervicalis
C. external laryngeal nerve
D. hypoglossal nerve
E. internal laryngeal nerve

Correct Answer: C
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The external laryngeal nerve, a branch of the superior laryngeal nerve from the vagus, innervates the cricothyroid muscle. Normally, the cricothyroid muscle varies the length and tension of the vocal cord, and in its absence, the voice acquires a monotonous quality. The accessory nerve (XI, choice A) only innervates the sternocleidomastoid and the trapezius muscles in the neck. The ansa cervicalis (choice B) supplies motor branches to the infrahyoid muscles. The hypoglossal nerve (XII, choice D) innervates intrinsic and extrinsic muscle fibers of the tongue. The internal laryngeal nerve (choice E) provides sensory innervation to the interior of the larynx.

QUESTION 87
Secretion of pulmonary surfactant is a function of which of the following?

A. alveolar dust cells
B. endothelial cells of capillaries in the alveolar septum
C. small granule cells
D. type I pneumocytes (squamous alveolar cells)
E. type II pneumocytes (greater alveolar cells)

Correct Answer: E
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
All the listed cell types are components of the respiratory system. Type II pneumocytes are the source of pulmonary surfactant. Alveolar dust cells (choice A) are macrophages. Endothelial cells (choice B) and type I pneumocytes (choice D) are components of the blood-air barrier. Small granule cells (choice C), which are members of the diffuse neuroendocrine system, function in paracrine and endocrine signaling.

QUESTION 88
Climbing fibers provide excitation to the deep cerebellar nuclei and the Purkinje neurons. The climbing fibers originate from which of the following structures?

A. inferior olivary nucleus
B. pontine nuclei
C. spinal cord
D. superior olivary nucleus
E. vestibular nuclei

Correct Answer: A
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The inferior olivary nucleus in the medulla oblongata is the sole source of climbing fibers to the cerebellum. All other sources of fibers to the cerebellum such as the pontine nuclei (choice B), spinal cord (choice C), or vestibular nuclei (choice E) provide mossy fibers to the cerebellum. The superior olivary nucleus (choice D) receives auditory fibers from the cochlear nuclei and projects back to the cochlea by way of the olivocochlear bundle. It modifies the sensory input from the organ of Corti in the cochlea and is not involved with cerebellar circuitry.

QUESTION 89
A newborn infant suffers from epidermolysis bullosa simplex, characterized by skin blistering soon after birth. The blisters appear at sites of pressure or rubbing such as the fingers. You explain to the distressed parents that this condition is a disease of intermediate filaments and results from mutant genes for keratins K5 and K14. Which cells of the skin normally produce keratins K5 and K14?

A. adipose cells in the hypodermis
B. basal cells of the epidermis
C. fibrocytes of the dermis
D. melanocytes of the epidermis
E. upper differentiating cells of the epidermis

Correct Answer: B
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
Basal cells of the epidermis produces keratins K5 and K14. Adipose cells in the hypodermis (choice A), fibrocytes of the dermis (choice C), and melanocytes of the

epidermis (choice D) do not synthesize keratins. Upper differentiating cells of the epidermis (choice E) produce keratins K1 and K10. A keratin K9 is also found in the palmar or plantar regions of the epidermis.

QUESTION 90
Cell adhesion molecules enable intercellular contacts in epithelial as well as nonepithelial cells. Which of the following cell adhesion molecules are calcium-dependent molecules?

A. disintegrins
B. integrins
C. intercellular adhesion molecules (I-CAM)
D. neural cell adhesion molecules (N-CAM)
E. selectins

Correct Answer: E
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
Cell adhesion molecules are divided into two major classes on the basis of their dependence on calcium. Calcium-dependent cell adhesion molecules are the cadherins and the selectins. Calcium- independent cell adhesion molecules include members of the immunoglobulin superfamily, the I-CAM (choice C), and the N-CAM, as well as the integrins (choice B). Disintegrins (choice A) are found in snake venom and disrupt the integrin-mediated cell binding to extracellular matrix proteins such as laminin or fibronectin.

QUESTION 91
After removal of cancerous lymph nodes from the lateral pelvic wall, a patient develops painful spasms of the adductor muscles and sensory deficits in the medial thigh region. The adductor muscles are innervated by which of the following nerves?

A. femoral
B. inferior gluteal
C. obturator
D. pudendal
E. sciatic

Correct Answer: C
Section: Anatomy
Explanation

Explanation/Reference:

Explanation:
The obturator nerve innervates the adductor muscles and the medial region of the thigh. The nerve originates from the lumbar plexus, runs on the lateral aspect of the pelvic wall, and exits through the obturator canal to reach the medial aspect of the thigh. Lying on the lateral pelvic wall, it may be injured by surgical mishap. The femoral nerve (choice A) innervates the anterior aspect of the thigh and the muscles contained within the sartorius and the quadriceps femoris. The inferior gluteal nerve (choice B) innervates the gluteus maximus muscle and is confined to the gluteal region. The pudendal nerve (choice D) is sensory to the genitalia, motor to the perineal muscles, the external urethral sphincter, and the external anal sphincter. The sciatic nerve (choice E) innervates the hamstring muscles in the posterior aspect of the thigh.

QUESTION 92
A renal calculus (kidney stone) passing from the renal pelvis into the ureter causes excessive distention and severe ureteric colic. During development in the embryo, the ureter arose from which of the following?

A. mesonephric duct
B. metanephric diverticulum
C. metanephric mass of intermediate mesoderm
D. paramesonephric duct
E. pronephric duct

Correct Answer: B
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The metanephric diverticulum or ureteric bud gives rise to the ureter, renal pelvis, calices, and collecting tubules. The metanephric mass of intermediate mesoderm (choice C) gives rise to the nephrons in the kidney. The mesonephric and paramesonephric ducts (choices Aand D) play essential roles in the development of the male and female reproductive system, respectively. The pronephric duct (choice E) is derived from the transitory, nonfunctional first set of kidneys or pronephroi and does not contribute to the development of the ureter.

QUESTION 93
A patient suffering from Charcot-Marie-Tooth disease displays progressive degeneration of peripheral nerves, distal muscle weakness and atrophy, and defects in deep tendon reflexes. This condition is associated with an abnormal mutation in the gene encoding connexin-32. Connexins are normally found in which type of cell junctions?

A. communicating (gap) junction
B. hemidesmosome
C. macula adherens (spot desmosome)
D. occluding (tight) junction
E. zonula adherens (belt desmosome)

Correct Answer: A
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
Communicating (gap) junctions are formed by connexins, which associate together in groups of six to form connexons. The alignment of connexions between two cells allows for direct channels of communication between their cytoplasms, facilitating the transfer of molecules such as calcium or cyclic adenosine monophosphate (cAMP). Hemidesmosome (choice B), macula adherens (spot desmosome; choice C), and zonula adherens (belt desmosome; choice E) are classified as anchoring junctions. They are associated with intermediate filaments (hemidesmosome and macula adherens) or with actin microfilaments (zonula adherens), but not connexins. Occluding (tight) junctions (choice D) contain the proteins occludin and claudin but not connexin.

QUESTION 94
Calcitonin decreases blood calcium and boneresorbing activity in which of the following?

A. osteoblast
B. osteoclast
C. osteocyte
D. osteon
E. osteoprogenitor cells

Correct Answer: B
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
Calcitonin reduces the surface ruffling of osteoclasts and their activity. Osteoclasts are formed by fusion of blood monocyte derivatives and are components of the mononuclear phagocyte system. Under the influence of parathyroid hormone, osteoclasts enlarge their ruffled borders and increase their bone-resorbing activity. Osteoprogenitor cells (choice E), osteoblast (choice A), and osteocyte (choice C) are bone-forming cells. Osteon (choice D) is another name for the haversian system which is the haversian canal, its contents, surrounding lamellae, and osteocytes.

QUESTION 95
During development, which of the following structures act as a temporary set of kidneys in the fetus?

A. mesonephroi
B. metanephroi
C. paramesonephric ducts

D. pronephroi
E. ureteric bud

Correct Answer: A
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The second set or mesonephroi appear late in the fourth week and are functional until the permanent kidneys or metanephroi are fully developed. During development, three sets of kidneys are formed in the embryo. The first set or pronephroi (choice D) are transitional, nonfunctional structures that appear around the fourth week of development. Next come the mesonephroi, then the permanent set of kidneys develops from the metanephroi. The paramesonephric ducts (choice C) are structures developing lateral to the gonads and mesonephric ducts. They play an essential role in the female reproductive system, but are not involved in the formation of the kidneys. The ureteric bud (choice E) is an outgrowth from the mesonephric duct that gives rise to the ureter, renal pelvis, calices, and collecting tubules.

QUESTION 96
In adults, lack of vitamin D gives rise to the disease osteomalacia characterized by progressive softening and bending of the bones. This is due to a defect in the mineralization of the osteoid. Under normal conditions, the osteoid is found along which of the following locations?

A. the interface between osteocytes and bones
B. the interface between osteoprogenitor cells and bone marrow
C. the interface between the fibroblasts in the periosteum
D. the interface between the osteoblast and bone
E. the ruffled border of osteoclasts

Correct Answer: D
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
Osteoid is the unmineralized organic matrix formed by osteoblasts and found at the interface between these cells and bone. Osteocytes (choice A) are surrounded by bone and no longer manufacture osteoid. Osteoprogenitor cells (choice B) are similar to stem cells and do not manufacture bone material. Fibroblasts (choice C) are cells of connective tissue forming the periosteum and not bone. Osteoclasts (choice E) are bone-resorbing cells.

QUESTION 97
Lymph nodes are populated by lymphocytes that exit the vascular compartment to gain access to the parenchyma of the node by passing through the walls of which of the following?

A. afferent lymphatic vessels
B. arterioles
C. efferent lymphatic vessels
D. high endothelial postcapillary venules
E. medullary sinuses

Correct Answer: D
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
High endothelial venules (HEV), located primarily in the deep cortex, are specialized to recruit circulating lymphocytes from the blood. Lymphocytes in the circulating blood adhere to the lining endothelial cells of HEV by way of an integrin-based recognition. Lymphocytes then gain access to the lymph node tissue by actively migrating (a process called diapedesis) between or through endothelial cells. Afferent lymphatic vessels (choice A) conduct lymph, not blood, into the lymph node. The source of the lymph is either upstream lymph nodes or tissue fluid from the region supplied by the node. This component of the system serves as a filter and as a mechanism for antigen-presenting cells to enter the node. Arterioles (choice B) are a component of the circulation of the lymph node, but they are not permeable to cell traffic. Efferent lymphatic vessels (choice C) conduct lymph and cells from the lymph node to either the blood circulation or downstream lymph nodes. Lymph in efferent lymphatic vessels conveys immunoglobulins and recirculating lymphocytes to the bloodstream. Medullary sinuses (choice E) are part of a system of passages that filter lymph and direct it from the afferent lymphatic vessels to the efferent lymphatic vessels. Medullary sinuses occupy spaces between medullary cords, which are occupied by large numbers of plasma cells, the cells that secrete immunoglobulins.

QUESTION 98
A 32-year-old female professional gardener complains of increasing muscle weakness and fatigue during the day, requiring her to take frequent rests. She also reports that she cannot enjoy her meals any more because her muscles of mastication quickly weaken and she has to stop chewing. When she watches television at night for a long period of time, her vision becomes blurry and she sees double. Her neurologist makes a preliminary diagnosis of myasthenia gravis. Which of the following is the cause of myasthenia gravis?

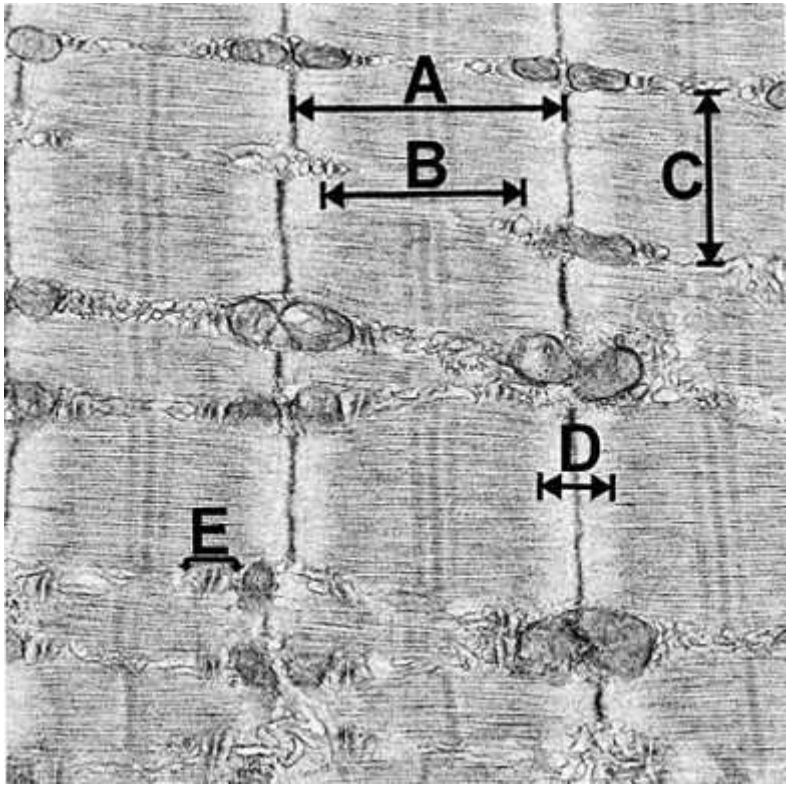
A. Acetylcholine synthesis in motor neurons is impaired.
B. Acetylcholinesterase synthesis is inhibited.
C. Autoantibodies destroy cholinergic receptors at the postsynaptic membrane preventing binding of acetylcholine.
D. Neurotransmitter release is impaired at the presynaptic membrane of the neuromuscular junction.
E. Signal transduction within the muscle is impaired.

Correct Answer: C
Section: Anatomy
Explanation

Explanation/Reference:

Explanation:
Myasthenia gravis is an autoimmune disorder where autoantibodies target the postsynaptic cholinergic receptors and destroy them. Acetylcholine released from motor neurons is thus unable to bind and the muscle contraction weakens due to decreased neurotransmitter communication. Acetylcholine synthesis in motor neurons (choice A) remains normal. Acetylcholinesterase (choice B) is the enzyme which degrades acetylcholine and its synthesis is not affected in myasthenia gravis. The cholinergic neurotransmitter release mechanism (choice D) at the presynaptic membrane, as well as the signal transduction mechanism (choice E) within the muscle, remain normal.

QUESTION 99
In Fig. following figure which labeled bracket spans a sarcomere?



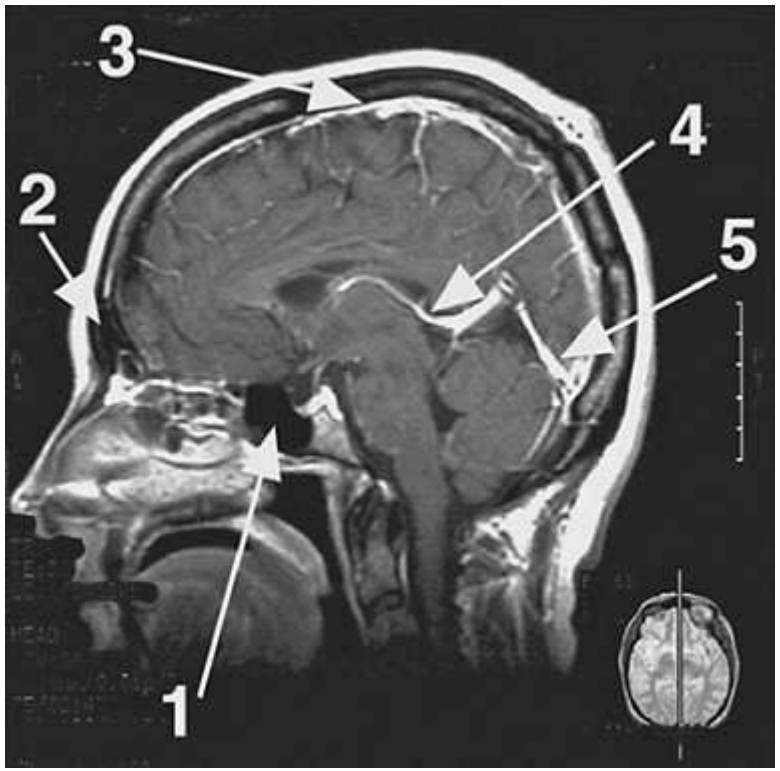
A. A
B. B
C. C
D. D

E. E

Correct Answer: A
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
An individual sarcomere, the unit of contraction in striated muscle, spans the interval between successive Z lines. Each sarcomere encompasses an A-band (choice B) and half of each of two I bands (choice D). Each myofibril (choice C) of a striated muscle fiber is composed of a tandem series of sarcomeres. Coupling of excitation and contraction is a critical function of the triad (choice E), which is composed of a T tubule interposed between two cisternae of the sarcoplasmic reticulum.

QUESTION 100
The great cerebral vein of Galen indicated by arrow 4 in following figure is formed by the union of two internal cerebral veins and drains into which of the following?

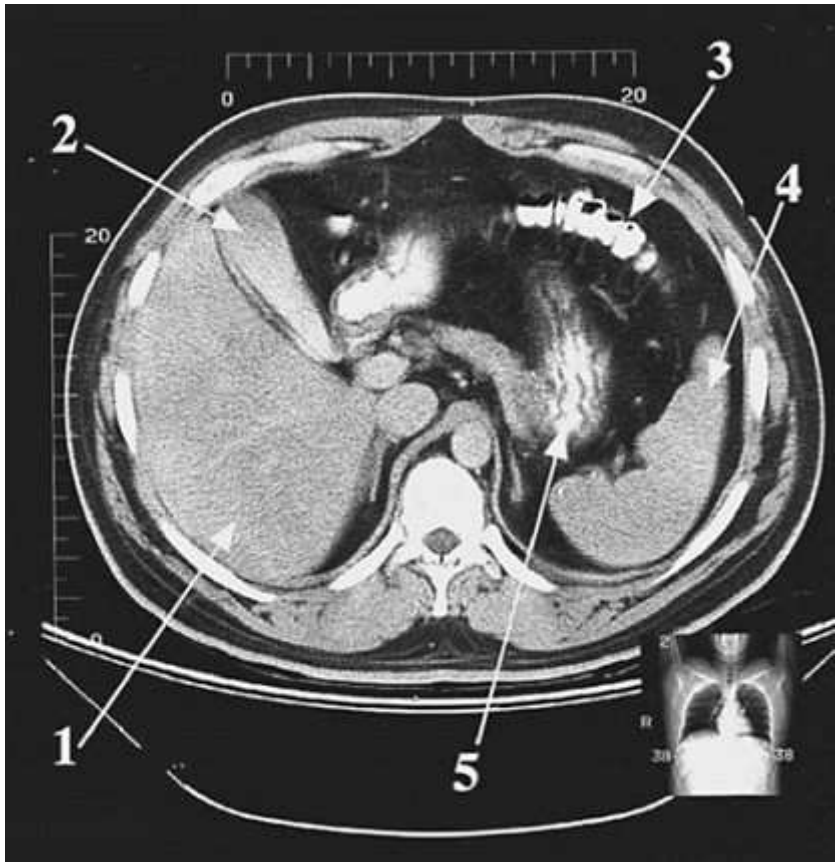


A. confluence of sinuses
B. frontal sinus
C. sphenoid sinus
D. straight sinus
E. superior sagittal sinus

Correct Answer: D
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The great cerebral vein of Galen (arrow 4) drains posteriorly into the straight sinus (arrow 5). The union of the superior sagittal sinus (choice E; arrow 3) and the straight sinus forms the confluence of sinuses (choice A). The straight sinus and superior sagittal sinus are dural venous sinuses: they contain venous blood draining form the brain, skull, and scalp. The frontal sinus (choice B) and the sphenoid sinus (choice C) are bony sinuses: they are hollow, airfilled structures and do not drain venous blood.

QUESTION 101
A 42-year-old female patient has to undergo emergency cholecystectomy due to intense biliary colic. The structure to be removed during the surgery is indicated in following figure by which of the following arrows?



A. 1
B. 2
C. 3
D. 4
E. 5

Correct Answer: B
Section: Anatomy
Explanation

Explanation/Reference:

Explanation:
Arrow 2 points to the gallbladder, which will be removed during the cholecystectomy (surgical removal of the gallbladder). Biliary colic may be due to impaction of a gallstone in the cystic duct, resulting in cholecystitis (inflammation of the gallbladder). Arrow 1 (choice A) points to the liver. Arrow 3 (choice C) points to the transverse colon. Arrow 4 (choice D) points to the spleen and arrow 5 (choice E) indicates the stomach, recognizable by its internal rugae.

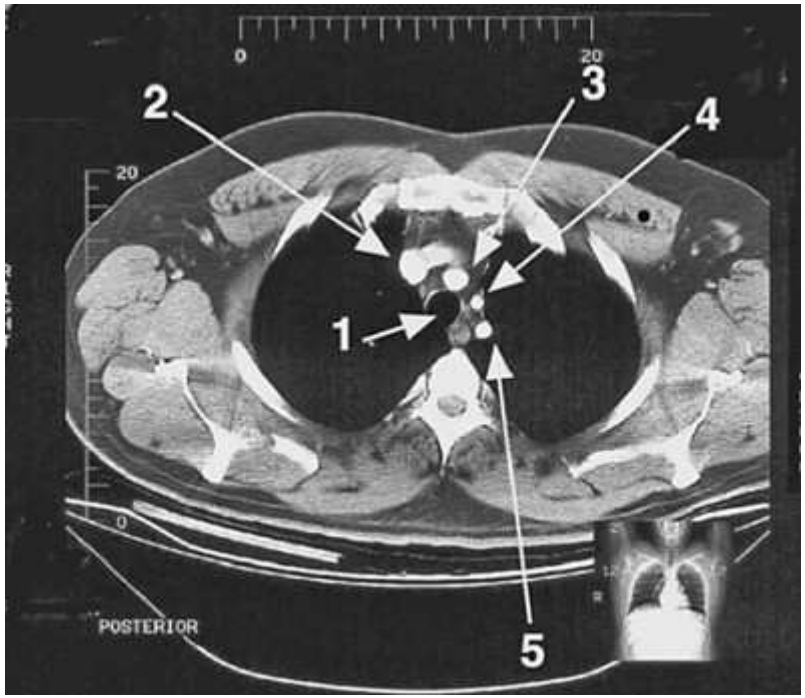
QUESTION 102
Apatient with a developing astroglioma in the primary auditory cortex (Brodmann's area 41) complains of hearing unusual noises. What is the main source of subcortical input to the primary auditory cortex?

A. inferior colliculus
B. lateral geniculate nucleus
C. medial geniculate nucleus
D. superior colliculus
E. superior olivary nucleus

Correct Answer: C
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The main subcortical afferents to the primary auditory cortex (Brodmann's area 41) arise from the medial geniculate nucleus of the thalamus. The inferior colliculus (choice A) is a midbrain auditory relay nucleus, which sends projections to the medial geniculate nucleus. The lateral geniculate nucleus (choice B) is a visual relay nucleus in the thalamus and it projects to the primary visual cortex (Brodmann's area 17). The superior colliculus (choice D) is a midbrain visual relay nucleus, which provides fibers to the tectospinal tract. The superior olivary nucleus (choice E) is a medullary auditory relay nucleus, which sends projections to the cochlea.

QUESTION 103
A 65-year-old male patient develops neurological symptoms due to an embolus in the left common carotid artery. In the CT scan in following figure, the involved vessel is indicated by which of the following arrows?



A. 1
B. 2
C. 3
D. 4
E. 5

Correct Answer: D
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
Arrow 4 points to the left common carotid artery. The three arteries arising from the arch of the aorta are lined anteriorly to posteriorly on a slanted line: arrow 3 (choice C) shows the brachiocephalic artery, arrow 4 (choice D) points to the left common carotid artery, and arrow 5 (choice E) indicates the left subclavian artery. Arrow 2 (choice B) points to the right brachiocephalic vein, which is joined here by the left brachiocephalic vein. Arrow 1 (choice A) points to the trachea, which is filled with air and thus is not radiopaque.

QUESTION 104
A 53-year-old male patient has developed an abnormal hypersensitivity in the face area. He complains that he feels pain when he drives with the window down and from the wind blowing on his face. The pain is exacerbated by direct touch to the left side of his lower jaw. The patient is diagnosed with trigeminal neuralgia (tic douloureux). Where do pain fibers from the left side of his mandible project to?

A. mesencephalic trigeminal nucleus
B. motor trigeminal nucleus
C. principal sensory trigeminal nucleus
D. spinal (descending) trigeminal nucleus
E. trigeminal (gasserian) ganglion

Correct Answer: D
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
Fibers from pain and temperature receptors in the face area all project to the spinal (descending) trigeminal nucleus. The mesencephalic trigeminal nucleus (choice A) contains the perikarya of the proprioceptive fibers of the muscles of mastication. The motor trigeminal nucleus (choice B) receives innervations from the mesencephalic trigeminal nucleus. The principal sensory trigeminal nucleus (choice C) receives somatosensory fibers from the face, gums, teeth, and anterior two-thirds of the tongue. The trigeminal (gasserian) ganglion (choice E) contains the sensory perikarya of all three subdivisions of the trigeminal nerve.

QUESTION 105
Askydiver landing forcefully on his right lower limb suffered a central fracture of the acetabulum with dislocation of the femoral head into the pelvis. The acetabulum is formed by the joining of the ilium, ischium, and pubis. These three bones are completely fused by which of the following periods?

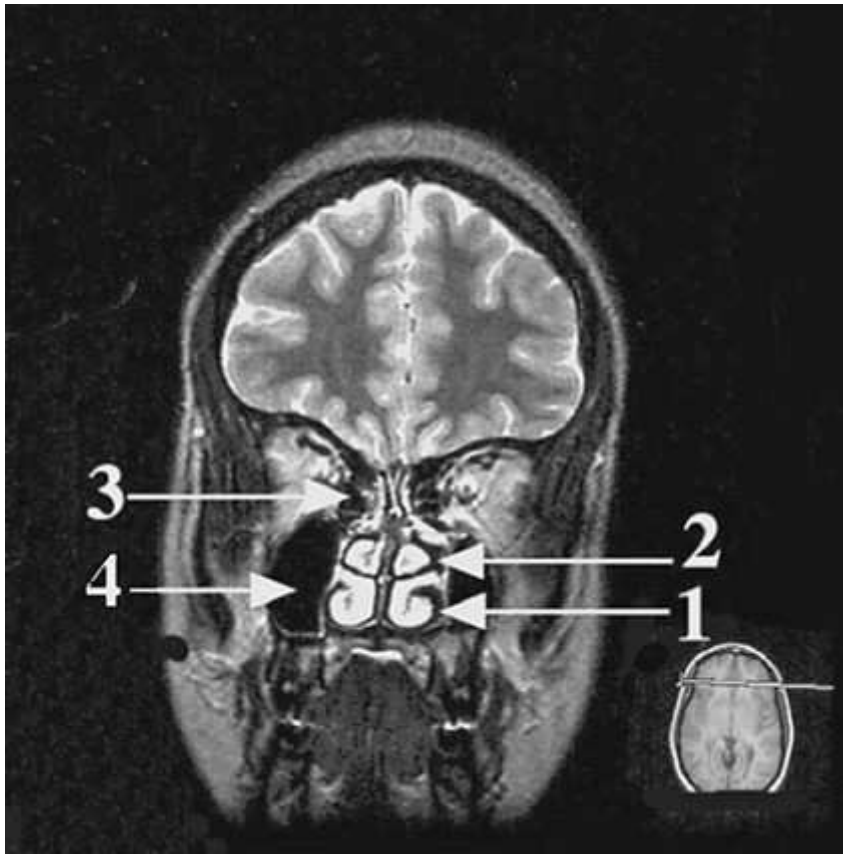
A. birth
B. 6 years
C. puberty
D. 16 years
E. 23 years

Correct Answer: E
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:

Fusion of the ilium, ischium, and pubis at the acetabulum is usually complete by age 23. From birth to the early 20s (choices AD), the three bones are held together by a Y-shaped cartilage.

QUESTION 106
In the coronal section of the head shown in following figure arrow 2 points to a structure that belongs to which of the following?



A. ethmoid bone
B. inferior nasal concha
C. maxillary bone
D. nasal septum
E. vomer bone

Correct Answer: A
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
Arrow 2 points to the middle nasal concha, which is part of the ethmoid bone. Arrow 3 points to the ethmoid sinus, which also belongs to the ethmoid bone. The inferior nasal concha (arrow 1) is a separate bone (choice B). The maxillary bone (choice C) is located more laterally and does not contribute to the nasal conchae. The maxillary sinus, a part of the maxillary bone, is indicated by arrow
4. The vomer bone (choice E) forms part of the nasal septum (choice D), which can be seen here as the thin line between the nasal conchae. The nasal conchae have no attachment to the septum.

QUESTION 107
The hands and nails of a 45-year-old woman show the discolorations indicated in below figure. 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?

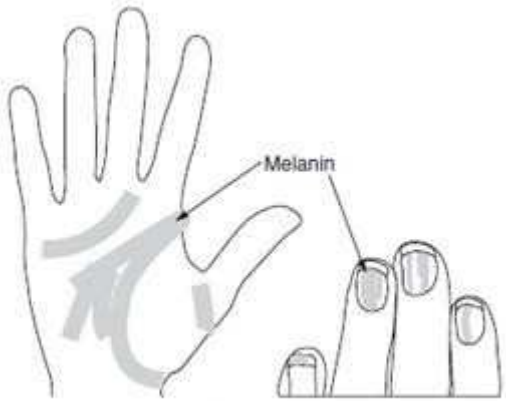


FIG. 2-1

A. adrenocorticotropic hormone (ACTH) secretion
B. corticotrophin-releasing hormone (CRH) secretion
C. insulin sensitivity in muscle
D. protein degradation
E. wound healing

Correct Answer: D
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
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.

QUESTION 108
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

Correct Answer: C
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
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.

QUESTION 109
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

Correct Answer: B
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
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.

QUESTION 110
End-stage chronic renal disease is associated with a glomerular filtration rate (GFR) of less than 15 mL/min and an increase in which of the following blood values?

A. calcium

B. erythropoietin (EPO)
C. hematocrit
D. phosphate
E. 1,25-(OH vitamin

Correct Answer: D
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
Chronic renal failure reduces phosphate excretion and thus phosphate accumulates in the blood. The renal peritubular cells are the major source of circulating EPO, which stimulates red blood cell production. Hence renal failure will decrease EPO levels (choice C) and will decrease hematocrit (choice E) as well. The kidney is responsible for production of vitamin D3, the active

$1{,}25-(\mathrm{OH})_2$

form of vitamin D, and renal failure also results in decreased active vitamin D (choice E). Secondary to this, the circulating levels of calcium will decrease (choice A).

QUESTION 111
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

Correct Answer: E
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
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 18.524.9), 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).

QUESTION 112
The ventricular action potential labeled N in below figure represents a normal ventricular action potential. Which of the other action potentials (labeled AE) would be most characteristic of the ventricular cell after administration of a drug that partially blocks slow calcium channels?

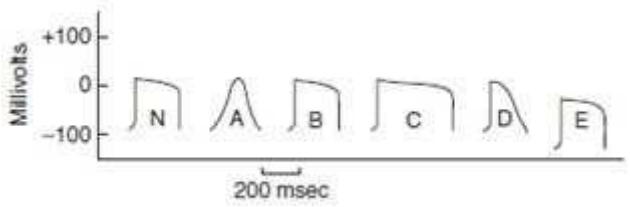


FIG. 2-2

A. A
B. B
C. C
D. D
E. E

Correct Answer: D
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
The slow calcium channels function in the ventricular myocardial cell to allow the influx of calcium into the cell, which has the dual role of triggering the calcium-mediated contractile mechanism and maintaining the depolarized state after the voltage-gated sodium channels close, soon after the rapid upstroke. Hence, blocking these channels will shorten the plateau phase of the action potential as seen in choice D, while also decreasing the contractile force of the heart. In choice A action potential duration is also shortened, but in a manner that would reflect blockade of the rapid voltagegated sodium channels, not the slow calcium channels. Choice B represents no change in the action potential. Choice C would occur if the drug prolonged the open state of the slow calcium channels. The hyperpolarization of choice E is more likely the result of increased potassium channel currents.

QUESTION 113
Pupil size is an important indicator of brainstem function. Which of the following results in papillary 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

Correct Answer: E
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
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).

QUESTION 114
For the bithermal caloric test, a measure of vestibular sensitivity, warm or cold water is introduced into the ear. This often causes vertigo and nausea as a side effect as a result of which of the following?

A. convection currents in endolymph
B. especially fast flow of endolymph
C. temporary immobilization of cristae ampullares
D. temporary immobilization of otolith organs
E. temporary inhibition of cochlear hair cells

Correct Answer: A
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
Water that is either warmer or cooler than body temperature when introduced into the external auditory meatus sets up convection currents within the endolymph of the inner ear. These currents may result in the movement of the cupula, the gelatinous matrix, which sits atop the crista ampullaris and occludes the lumen of the semicircular canal. Displacement of the cupula results in activation of the vestibular hair cells of the ampullar crista. This inappropriate stimulation of the vestibular system conflicts with sensory information from other sensor organs, including vestibular sensors on the contralateral side, vision, and proprioception, and may in

turn result in vertigo and nausea. The existence of the many ducts within the inner ear might imply that the fluids that fill them are flowing through the ear. However, neither endolymph nor perilymph "flow" along their respective compartments in the normal or stimulated vestibular system (choice B). Neither hair cells of cristae ampullares (choice C) nor of otholith organs (choice D) nor of the cochlea (choice E) are temporarily immobilized or inhibited by temperature changes.

QUESTION 115
below figure shows a lead II electrocardiogram from a normal 30-year-old female at rest. If a beta- adrenergic agonist such as isoproterenol is administered intravenously to this woman, what will be her resulting heart rate in beats per minute?

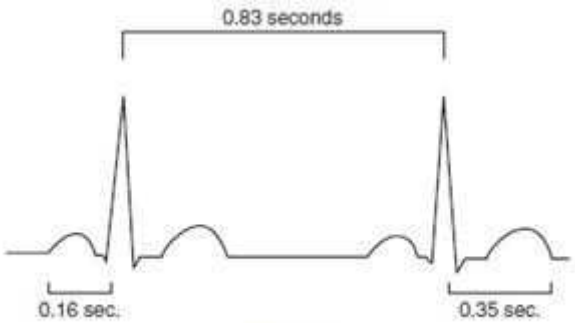


FIG. 2-3

A. 40
B. 55
C. 65
D. 70
E. 90

Correct Answer: E
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
From inspection of the figure, the R-R interval (time between heart beats) at rest is 0.83 seconds; 60 seconds/minute divided by 0.83 yields a resting heart rate of 72 beats/minute. Since activation of

β_1

receptors in the sinoatrial node will result in increased heart rate, the only alternative larger than 72 beats/minute is E., 90 beats/minute.

QUESTION 116
With increasing age, it is quite common for adults to have very low sensitivity for highpitch sounds. Which of the following physiologic responses occur as the pitch of a sound is increased at constant sound pressure?

A. a greater number of hair cells become activated
B. the amplitude of maximal basilar membrane displacement increases
C. the frequency of action potentials in auditory nerve fibers increases
D. the location of maximal basilar membrane displacement moves toward the cochlear base
E. units in the auditory nerve become responsive to a wider range of sound frequencies

Correct Answer: D
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
The primary change in the cochlea due to an increase in the frequency of a sound wave is a change in the position of maximal displacement of the basilar membrane. A low-pitched sound produces the greatest displacement toward the apex of the cochlea, which results in activation of hair cells at that location. As pitch increases, the position of greatest displacement moves closer to the base of the cochlea. Increases in the number of hair cells that are activated (choice A), increased amplitude of basilar membrane displacement (choice B), increases in the frequency of discharge of units in the auditory nerve fibers (choice C), and an increase in range of frequencies to which such units respond (choice E), are all more likely to be observed in response to increases in the intensity of the sound stimulus (sound pressure) rather than to increases in pitch.

QUESTION 117
A 20-year-old woman admits herself to the emergency room with a yellow discoloration of the whites of her eyes. She says that she does not drink and that she has not experienced any changes in her stool. Her liver enzyme profile and direct serum bilirubin levels are normal, while total bilirubin is elevated.
What is the most likely cause for her jaundice?

A. defect in hepatocytes
B. defect in Kupffer cells
C. gallstones
D. hemolysis
E. tumor obstructing bile duct

Correct Answer: D
Section: Physiology
Explanation

Explanation/Reference:

Explanation:
Rupture of large numbers of red blood cells can result in jaundice in the absence of any liver disease. The capacity of the liver to clear released heme metabolites such as bilirubin is temporarily exceeded. Since the liver will not perform its normal function to conjugate bilirubin before excretion in bile and urine, unconjugated bilirubin backs up in serum. This is the reason for the increase in total bilirubin, while conjugated bilirubin, also called direct bilirubin, is not affected. Direct bilirubin would be elevated with most defects of liver cells (choice A) and with obstruction of bile flow by gallstones (choice C) or by a tumor (choice E). All these would most likely also affect bile formation and consequently absorption of dietary fat and fat-soluble vitamins, with the consequence of developing oily, fatty stool. Kupffer cells (choice B) are macrophages within the liver and don't play a role in the production of bilirubin.

QUESTION 118
A 54-year-old insulin-dependent diabetic notes that her insulin requirements have gone up dramatically in the past year (from 50 U to nearly 200 U of recombinant human insulin) and her blood glucose is still poorly controlled. A possible explanation for the worsening of her diabetes includes which of the following?

A. a high titer of anti-insulin antibodies
B. an improved diet
C. an improved exercise program
D. progression of macrovascular disease
E. weight loss

Correct Answer: A
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
The patient clearly has an increase in her state of insulin resistance. Given the magnitude of her increased insulin requirements, she most likely developed a high titer of antiinsulin antibodies that are preventing the injected insulin from lowering blood glucose effectively. Agood choice of lifestyle, including an improved diet (choice B), an improved exercise program (choice C), or weight loss (choice E) each are shown to beneficially affect her insulin requirements. Progression of macrovascular disease (choice D) is largely irrelevant to her insulin requirements, except to the extent that it might decrease her ability to exercise.

QUESTION 119
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

Correct Answer: E
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
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).

QUESTION 120
An advertisement promotes energy bars containing fructose as an ideal food to take on extreme mountain-climbing expeditions. Which of the following statements concerning fructose absorption is true?

A. absorption of fructose into an intestinal epithelial cell is by facilitated transport and thus does not require energy
B. metabolism of fructose generates more energy than glucose
C. some fructose is already absorbed in the mouth and hence is the fastest way to get energy
D. the presence of fructose aids in absorption of vitamin A, C, and D
E. the presence of fructose inhibits reabsorption of glucose, which is then more readily available for muscle activity

Correct Answer: A
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
Carbohydrate absorption occurs at enterocytes of the upper region of small intestinal villi. Fructose absorption is via the facilitated transporters GLUT5 across the apical enterocyte membrane and GLUT2 across the basolateral enterocyte. Glucose and galactose on the other hand are transported into enterocytes on carriers in combination with a sodium ion. The energy for this secondary active transport is provided by the electrochemical sodium gradient that is created by Na/K-ATPases. Experimental conditions that collapse the sodium electrochemical gradient, hypoxia, or poisoning of the Na-KATPase by ouabain inhibit glucose, but not fructose absorption. Nevertheless, the physiological importance of "saving energy" under extreme conditions such as mountain climbing through the use of fructose as energy source is questionable. For instance, fructose absorption is much slower than absorption of glucose and galactose. The statements in choices B, C, D, and E are incorrect.

QUESTION 121
A patient with untreated diabetes mellitus is admitted to the hospital for treatment. Laboratory findings include a blood pH below 7.2. Which of the following is likely

to directly result from this level of acidemia?

A. arteriolar constriction
B. decreased catabolism
C. hyperkalemia
D. hypoventilation
E. insulin sensitivity

Correct Answer: C
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
Acidemia is the presence of excess ions in blood, which tends to create a rise in the extracellular

H^+

potassium concentration. The rule of thumb for an inorganic acid that causes the acidity is that a decrease in pH of 0.1 unit leads to a rise in plasma potassium of 0.6 milliequivalents per liter. The effect of an organic acid is a lot less. The mechanism responsible for the relationship between pH and extracellular potassium concentration is not completely understood. One effect is that the intracellular acidosis inhibits influx by reducing the activity of the Na-K-pump. An exchange of extracellular

K^+

for intracellular might also contribute. Choices A, B, D, and E are the opposite of what is

H^+

observed in acidemia.

QUESTION 122
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

Correct Answer: A
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
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.

QUESTION 123
Although most cases of hypertension are "essential," meaning the underlying disorder is unknown, about 10% of cases are "secondary hypertension" due to a specific, usually treatable cause. Which of the following alternatives can lead to secondary hypertension?

A. adrenal insufficiency
B. estrogen deficiency
C. hyperparathyroidism
D. renal artery stenosis
E. volume depletion

Correct Answer: D
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
A fixed lesion of the renal artery results in impaired perfusion. When the kidney is poorly perfused, it increases renin secretion, which increases blood pressure and thus improves renal blood flow. Hence the appropriate treatment is surgical correction of the renal artery lesion. Adrenal insufficiency (choice A), estrogen deficiency (choice B), and volume depletion (choice E) are situations that tend to diminish blood pressure. There is no clear relationship between hyperparathyroidism (choice C) and hypertension.

QUESTION 124
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

Correct Answer: D
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
In smooth muscle, increased cytoplasmic [ ] activates myosin light chain kinase, which acts to

Ca^{2+}

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 [

Ca^{2+}

] 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.

QUESTION 125
In which of the following conditions would the gas composition of both end pulmonary capillary blood and alveolar air approximate that of mixed venous blood?

A. airway obstruction
B. breathing 100% oxygen
C. hyperventilation
D. normal breathing
E. pulmonary capillary embolus

Correct Answer: A
Section: Physiology
Explanation

Explanation/Reference:
Explanation:

When the airway is obstructed, an alveolus will not be adequately ventilated. In this condition, effective gas exchange does not occur and alveolar gas composition and end pulmonary blood gas compositions approach 46 mm Hg and 44 mm Hg C --the gas composition of mixed venous blood. In normal

O_2

breathing (choice D) alveolar air equilibrates with pulmonary capillary blood, with a gas composition of approximately 100 mm Hg and 40 mm Hg C . With hyperventilation (choice C), C partial

O_2

pressure will fall and partial pressure may increase relative to the normal values quoted above.

O_2

With a pulmonary capillary embolus (choice E), blood flow to an alveolus or to a group of alveoli is blocked. In this case, efficient gas exchange does not occur and gas composition of alveolar air approximates that of tracheal air (150 mm Hg and 0 mm Hg C). This condition is referred to as

O_2

wasted ventilation. In a healthy individual, breathing 100% (choice B) will increase alveolar

O_2

partial pressure and thereby increase end pulmonary capillary partial pressure.

O_2

QUESTION 126
Below figure shows pulmonary function test tracings from a healthy person and a patient with pulmonary fibrosis. Of the following measures which would you expect to be increased in this patient, as compared to the expected norms?

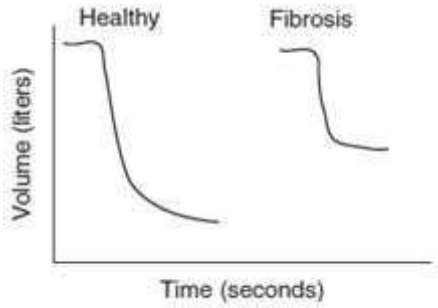


FIG. 2-12

A. Forced expiratory volume (FEV)/forced vital capacity (FVC)
B. FRC
C. FVC
D. tidal volume
E. vital capacity

Correct Answer: A
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
Pulmonary fibrosis is a restrictive lung disease. below figure illustrates pulmonary function testing data in a normal subject and a patient with fibrosis. Volume-time curves reveal and in both

FEV_1

subjects. The ratio, which is typically about 0.8, is increased in patients with pulmonary

FEV_1/FVC

fibrosis. Lung volumes such as vital capacity (choice E) are decreased. Patients with restrictive lung disease tend to exhibit shallow breathing, thus tidal volume is decreased (choice D). Increased elasticity causes a decrease in FRC, the mechanical balance point between lungs and chest wall (choice B). Though as noted above and illustrated in below figure the ratio is increased in patients

with pulmonary fibrosis, itself is decreased (choice C).

FVC

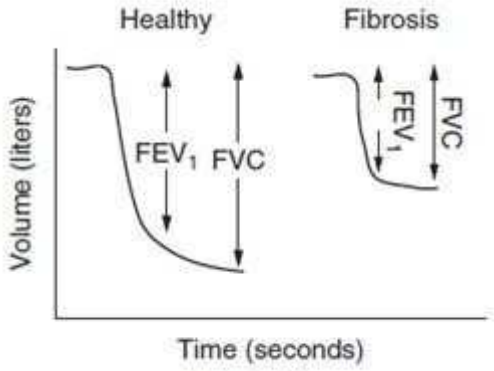


FIG. 2-29

QUESTION 127
A patient with chronic renal insufficiency due to renal vascular disease has a net functional loss of nephrons. If we assume that production of urea and creatinine is constant and that the patient is in a steady state, a 50% decrease in the normal GFR will cause which of the following to occur?

A. decrease plasma urea concentration
B. greatly increase plasma
C. increase the percent of filtered Na+ excreted
D. not affect plasma creatinine
E. significantly decrease plasma

Correct Answer: C
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
Both and excretion are tightly regulated. Thus, as GFR decreases in disease, the percentage

Na^+

of filtered or excreted increases to maintain a normal amount of or excretion

Na^+

(assuming Na+ and intake remain the same). Substances like urea (choice A) (some reabsorption)

K^+

and creatinine (choice D) (almost exclusively excreted by glomerular filtration) have no adaptive mechanisms to regulate plasma levels. Thus, a significant decrease in GFR results in significant increases in plasma creatinine and urea (assuming production of both substances remains constant). This is because the amount of substance x that is excreted (Ux·V) equals the amount produced. Furthermore, · V = GFR · Px. If GFR decreases, increases. Because of the increase in percent

U_x

filtered and that is excreted, an increase in plasma (choice B) or a decrease in plasma

Na^+

(choice E) would not be expected with a GFR that is 50% of normal. ÷ urine concentration of

K^+

x; ÷ plasma concentration of ; V ÷ urine volume.

P_x

QUESTION 128
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

Correct Answer: D
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
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.

QUESTION 129
A 30-year-old male seeks help because he lost weight and feels full after eating only a small amount of food. He is diagnosed with a delay in gastric emptying. Which of the following hormones has at physiological levels the strongest effect in inhibiting gastric emptying?

A. cholecystokinin
B. gastrin
C. glucose-dependent insulinotropic peptide
D. motilin
E. pancreatic polypeptide

Correct Answer: A
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
The major control mechanism for gastric emptying involves duodenal gastric feedback, hormonal as well as neural. The major hormone involved in the inhibition of gastric emptying is cholecystokinin (CCK), which is released by fat and protein digestion products. Gastrin (choice B) stimulates hydrochloric acid secretion and exerts a trophic effect on the gastric and intestinal mucosa. When the gastrin concentration is elevated to supraphysiologic levels, various other actions can be demonstrated including inhibition of gastric emptying. However, the physiologic importance of these actions is uncertain. Glucose-dependent insulinotropic peptide (GIP, choice C) is released from the intestinal mucosa by acid, fat, or hyperosmolarity and acts to some extent by inhibiting stomach functions including gastric motility. Although this function gave GIP its initial name (gastric inhibitory peptide), GIP's action as an enterogastrone is now controversial. The major physiologic action of GIP is to cause insulin release. Motilin (choice D) stimulates gastric motor activity, especially during the interdigestive phase, when it regulates contractions that serve to empty the GI residual contents. Pancreatic polypeptide (choice E) is a negative feedback regulator for pancreatic enzymes and bicarbonate secretion. It is considered to be a candidate hormone since it satisfies some, but not all of the criteria for hormonal status.

QUESTION 130
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--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

Correct Answer: D
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
In the adrenogenital syndrome, the failure to make cortisol due to lack of the adrenal enzyme 21-- 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.

QUESTION 131
A 59-year-old Caucasian female is self-donating blood in preparation for a hip replacement surgery in the near future. Shortly after her third session of donating a unit (pint) of whole blood, her mean arterial pressure remains unchanged, even though the venous return of blood to her heart is diminished. Which of the following is the most likely reason for the preservation of arterial pressure?

A. cardiac output rises to compensate for the reduced venous return
B. end-diastolic ventricular filling pressure rises during hemorrhage
C. fall in venous return is offset by an increase in total peripheral resistance
D. heart rate rises to compensate for a reduced venous return
E. venous return and blood pressure are unrelated

Correct Answer: C
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
By Ohm's law, a reduction in flow should also reduce pressure if resistance is constant. Therefore a rise in total peripheral resistance in the face of reduced flow would account for the preservation of arterial pressure. Choice A is incorrect since cardiac output and venous return must rise and fall together. Choice B is incorrect since end-diastolic ventricular filling pressure falls with decreased venous return. Choice D is incorrect since heart rate can maintain pressure only if venous return is also maintained. Choice E is incorrect since Ohm's law states the inverse relationship of venous return and pressure.

QUESTION 132
A 35-year-old weight lifter, who has been injecting testosterone for muscle mass augmentation, is evaluated for sterility and found to have an extremely low sperm count. Which of the following is an effect of testosterone and contributes to the mentioned sterility?

A. activation of inhibin
B. feedback activation of leptin
C. feedback inhibition of GnRH
D. inhibition of seminal prostaglandins
E. lowered core temperature

Correct Answer: C
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
Testosterone directly inhibits the secretion of GnRH from the hypothalamus, which affects secretion of LH and FSH and consequently secretion of testosterone. To initiate spermatogenesis, both FSH and testosterone are necessary. To maintain spermatogenesis after puberty, extremely high concentrations of testosterone seem to be required. Systemically administered testosterone does not raise the androgen level in the testes to as great a degree and it additionally inhibits LH secretion. Consequently, the net effect is generally a decrease in sperm count. There are two forms of inhibin (choice A) that are produced by Sertoli cells in males. They are activated by FSH, not testosterone, and inhibit FSH secretion by a direct action on the pituitary. Testosterone has been shown to have a suppressive, not activating (choice B) effect on leptin production. Prostaglandins (choice D) are produced by seminal vesicles and found in large quantities in semen. They are not

known to play a role in spermatogenesis. They are believed to aid fertilization by reacting with female cervical mucus and to support smooth muscle movements in the uterus and fallopian tubes. Testosterone stimulates basic metabolic rate and can raise, not lower body core temperature (choice E). Excessive temperature of the testes can temporarily cause sterility.

QUESTION 133
Evaluating the cause for a coma can be challenging. As a first step, the causes can be divided into two broad categories, structural/ surgical and metabolic/medical reasons. Which of the following findings suggests a metabolic cause in a comatose patient?

A. failure to withdraw from painful stimuli
B. gross blood in the cerebrospinal fluid
C. impaired pupillary light responses
D. posturing of limbs
E. serum sodium of 115 meq/L

Correct Answer: E
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
Hyponatremia of this magnitude for any reason is likely to cause seizures and coma, especially if the deviation from normal occurred rapidly (e.g., over 1 or 2 days). Withdrawal from painful stimuli (choice A) is a normal reaction. If intact, it would have provided information on the intactness of sensation and motor reflexes on the tested side. However, lack of withdrawal would be consistent with either a structural or a metabolic cause of coma, and therefore does not help. Blood in the cerebral spinal fluid (choice B) in a nontraumatic lumbar puncture suggests a structural rather than a metabolic cause of coma. Pupillary light responses (choice C) are typically preserved in metabolic encephalopathies. Posturing of limbs (choice D) is suggestive of a focal process involving the brainstem or midbrain rather than a metabolic encephalopathy.

QUESTION 134
Exogenous peripherally injected insulin differs from endogenously secreted insulin in a number of aspects, including which of the following?

A. achieves a higher concentration in the periphery than in the liver, contrary to endogenous insulin
B. contains C-peptide, which is missing from secreted endogenous insulin
C. is able to bypass insulin resistance observed with endogenous insulin
D. is always extracted from animal sources and, therefore, is less effective due to sequence differences and anti-insulin antibodies
E. is in the form of proinsulin, whereas endogenous insulin has had C-peptide removed

Correct Answer: A
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
The concentration of exogenous insulin is higher at the site of injection in the periphery, compared to its concentration in the liver. On the other hand, endogenous insulin is higher concentrated in the liver than in the periphery. Insulin is normally secreted by the endocrine pancreas into the portal venous drainage. Thus, it passes through the liver before being seen by the periphery. Acertain fraction of insulin is extracted by the liver; so that the concentration of insulin seen by the liver is normally higher than that seen by the periphery. This discrepancy between exogenous and endogenous insulin might contribute to the problems experienced by diabetics such as hypertension and cardiovascular disease. Injected insulin is missing C-peptide (choice B), while endogenous insulin is cosecreted with C-peptide, the physiologic functions of which remain unknown. Injected insulin is biologically active and not in the proinsulin form (choice E). Exogenous insulin generally used today in the United States is recombinant human insulin, not from animal sources (choice D). The problem of developing anti- insulin antibodies is now rarer since the injected insulin is not from animals. Insulin resistance (choice C) is generally due to receptor downregulation or desensitization, or anti-insulin antibodies. Tissues become equally resistant to both the body's own (endogenous) and administered (exogenous) insulin.

QUESTION 135
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

Correct Answer: D
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
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).

QUESTION 136
The terminal ileum was removed from a 50-year-old woman during excision of a tumor. About 3 years later, the patient was admitted to the hospital. She is very pale. Hemoglobin is 9 g/dL, MCV (mean corpuscular volume) has increased to 110 (110 fL). The provisional diagnosis is a vitamin

m^3

deficiency. Which of the following vitamins is the most likely one causing the symptoms?

A. A
B. B1
C. B6
D. B12
E. K

Correct Answer: D
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
Deficiency of vitamin results in hematological, neurological, and GI effects. The hematologic

B_{12}

symptoms include a low red blood cell count with large-sized macrocytic red blood cells as described. Absorption of vitamin is relatively complicated. The large and not very lipophilic molecule is

B_{12}

released from food by the low pH of the stomach and pepsin digestion and binds to R protein (also called haptocorin). Pancreatic proteases digest these complexes and the liberated cobalamin (vitamin) now complexes with an intrinsic factor (which is produced by gastric parietal cells) and is

B_{12}

absorbed as such in the terminal ileum. Hence, vitamin absorption will be low in this patient.

B_{12}

Liver storage is thought to be sufficient for 36 years so that the 3-year latency of the anemia further supports a vitamin deficiency. The water-soluble vitamins and (choices B and C) are

B_{12}

absorbed in the duodenum by simple diffusion. Absorption of the lipid-soluble vitamins A and K (choices A and E) is supported by bile-acid mixed micelles, although vitamin Aand vitamin do not

K_3

heavily rely on bile acids and can also enter the enterocytes by simple diffusion. Additionally, of the stated choices, only vitamin deficiency is associated with anemia.

B_{12}

QUESTION 137
below figure illustrates uptake of two gases (nitrous oxide and carbon monoxide) from alveolar air to pulmonary capillary blood. Based on this information what can we conclude about carbon monoxide?

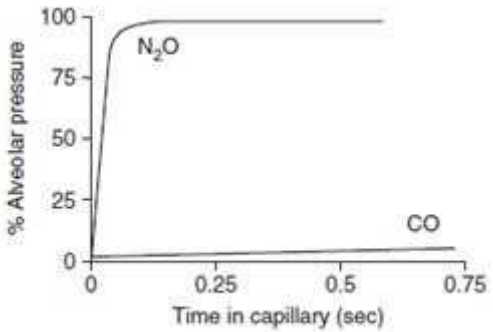


FIG. 2-13

A. it does not dissolve in blood
B. it does not interact with hemoglobin
C. it has equilibrated with pulmonary capillary blood
D. it is a diffusion-limited gas
E. it is a perfusion-limited gas

Correct Answer: D
Section: Physiology
Explanation

Explanation/Reference:
Explanation:

The plot shows that carbon monoxide fails to equilibrate with pulmonary capillary blood during the time that blood is exposed to alveolar air. Since pulmonary partial pressure rises to only a few percent of alveolar partial pressure, carbon monoxide is a diffusion-limited gas. In contrast, nitrous oxide, which does equilibrate, is a perfusion-limited gas (choice E). Carbon monoxide does cross the respiratory membrane (choice C), dissolve in pulmonary capillary blood (choice A), and binds with hemoglobin (choice B). In fact, its affinity for hemoglobin is about 250-fold greater than that of oxygen.

QUESTION 138
Which of the following is likely to cause a negative free-water clearance by the kidney?

A. central diabetes insipidus
B. demeclocycline, an inhibitor of the renal tubular actions of ADH
C. nephrogenic diabetes insipidus
D. water deprivation
E. water drinking

Correct Answer: D
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
Water deprivation will eventually increase extracellular fluid osmolality, which triggers release of ADH. ADH acts on the collecting duct to increase water reabsorption, thus making the excreted urine more concentrated via a negative free-water clearance. Choices B and C will reduce the sensitivity of the collecting duct to normal circulating ADH. Choices A and E will reduce the amount of ADH secreted by the posterior pituitary.

QUESTION 139
An 18-year-old woman presented with 1 week of history of fever and malaise. She had mild jaundice and elevated temperature. Hemoglobin was 13.8 g/dL, leukocyte count 13 × 109 per liter. Serum bilirubin was elevated (42 mmol/L) and contained 95% unconjugated bilirubin. Liver enzyme tests were normal. Which of the following is the most likely cause of these signs and symptoms?

A. alcohol poisoning
B. decreased glucuronyl transferase
C. increased lactate dehydrogenase (LDH)
D. excessive hemolysis
E. obstruction of bile flow

Correct Answer: B
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
Glucuronyl transferase is the enzyme that conjugates bilirubin in the liver, after which it is excreted in bile or urine. Ahereditary defect in glucuronyl transferase concentration, or activity, is called Gilbert syndrome. It may lead to mild jaundice and general discomfort with typical onset in childhood or early adulthood. Alcohol poisoning (choice A) leads to liver damage, and an elevation of conjugated bilirubin. Abnormalities of liver enzyme tests would be expected. Lactate dehydrogenase (choice C) catalyzes the conversion of lactate to pyruvate as part of cellular energy production. Since many cells including red blood cells are rich in LDH, increased serum LDH levels could point toward excessive hemolysis, but would not be a cause for it. Although hemolysis that exceeds the capacity of the liver to clear bilirubin from serum (choice D) would lead to increased unconjugated bilirubin, it is not the best choice due to the woman's normal hemoglobin (1216 g/dL for females). Obstruction of bile flow (choice E) leads to backup of largely conjugated bilirubin in the blood stream.

QUESTION 140
A 25-year-old male athlete has just completed a long distance bicycle race during a hot, humid day. At the conclusion of the race, he provides a urine sample for testing. Assuming that his fluid intake during the race was zero, in what portion of the nephron shown in below figure is the tubular fluid osmolality the lowest?

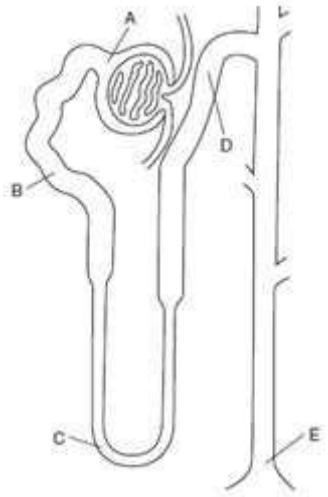


FIG. 2-14

A. A
B. B
C. C
D. D
E. E

Correct Answer: D
Section: Physiology

Explanation

Explanation/Reference:
Explanation:
The bicycle racer is likely dehydrated from his exercise and ADH would be secreted by the posterior pituitary in response to increased extracellular osmolality. The area of the nephron with the lowest osmolality will be the early distal tubule (choice D), a nephrondiluting segment. The fluid in Bowman's capsule (choice A) will be at the same osmolality as the plasma entering the glomerular capillaries. The fluid at the end of the proximal tubule (choice B) is isoosmotic with the Bowman's capsule fluid while the fluid in the thin descending loop of Henle (choice C) is greatly concentrated due to water reabsorption into the hyperosmotic medullary interstitium. The fluid at the end of the collecting duct (choice E) can be very concentrated or very dilute, but since ADH greatly increases water reabsorption in this segment, the fluid becomes very concentrated.

QUESTION 141
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

Correct Answer: C
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
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.

QUESTION 142
The parents bring a 5-month-old baby to the emergency room. It is their first child and they are insecure. The boy vomits frequently, seems to be constantly constipated, and has difficulties in defecation. A barium enema study reveals a region in the bowel that is collapsed and an enlarged colon above this area. Abiopsy from the part of the bowel 1 in above the anus is sent to the laboratory and histological analysis reveals the absence of ganglia in this tissue. What is the most likely diagnosis?

A. cholecystitis

B. gastroesophageal reflux disease
C. hirschsprung disease
D. polymyositis
E. temporary problem with no treatment required

Correct Answer: C
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
Hirschsprung disease is a genetic disorder caused by the absence of enteric nerve cells in the wall of the sigmoid colon and/or rectum. The portion of the bowel wall without nerve ganglia (aganglionic) cannot relax in response to bowel content so that the stool builds up behind the obstruction. In some children the problems begin shortly after birth, other infants are not acutely ill, but develop chronic symptoms such as constipation or anemia. Cholecystitis (choice A), caused by inflammation of the gallbladder, gastroesophageal reflux disease GERD (choice B), and polymyositis (choice D), a disorder affecting esophageal skeletal muscle, do not affect the neuronal regulation of the large intestine. Hirschsprung disease is almost always treated by surgical removal of the affected bowel segment and then joining the healthy bowel segments (choice E). A GI motility disorder might improve on its own due to the ability of the enteric nervous system in healthy GI tract portions to learn new motility patterns. However, it takes a very long time and the success is not certain.

QUESTION 143
Exhibit: *missing*
A healthy 27-year-old male is given a treadmill stress test. His cardiovascular values at rest and during exercise were:

	Rest	Exercise
Peak Systolic Blood Pressure (mm Hg)	105	140
Minimum Diastolic Blood Pressure (mm Hg)	75	65
Heart Rate (beats/min)	68	140

When compared to rest, what was the change in his arterial pulse pressure?

A. decreased from 140 to 65
B. increased from 30 to 75
C. increased from 68 to 140
D. increased from 115 to 140
E. remained unchanged since heart rate and systolic pressure both increased

Correct Answer: B

Section: Physiology
Explanation

Explanation/Reference:
Explanation:
By definition, arterial pulse pressure is the difference between peak systolic and minimum diastolic pressure. His resting pulse pressure was 105 - 75 = 30 and his exercise pulse pressure increased to 140
- 65 = 75.

QUESTION 144
A healthy 27-year-old male is given a treadmill stress test. His cardiovascular values at rest and during exercise were:
When compared to rest, what was the change in his estimated mean arterial pressure?

A. decreased by 10 mm Hg
B. increased by 5 mm Hg
C. increased by 25 mm Hg
D. increased by 35 mm Hg
E. increased by 140 mm Hg

Correct Answer: B
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
True mean arterial pressure cannot be determined without a pressure transducer, which averages the systolic and diastolic pressures throughout the cardiac cycle. However, mean arterial pressure can be estimated by adding one-third of pulse pressure to the minimum diastolic pressure. At rest his mean pressure is 30/3 + 75 = 85; during exercise mean pressure is 75/3 + 65 = 90. Hence, estimated mean pressure increased by 5 mm Hg.

QUESTION 145
Normal metabolism by the body generates large quantities of acid. In spite of this, normal blood pH is a slightly alkaline 7.4. This extracellular fluid alkalinity is maintained primarily by the body's removal of which of these?

A. ammonia
B. carbon dioxide
C. keto acids such a acetoacetic acid
D. lactic acid
E. titratable acids such as phosphoric acid

Correct Answer: B
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
The vast majority of metabolic acid excretion is in the form of the volatile acid carbon dioxide which is removed via the lungs. Much smaller quantities of nonvolatile acids must be excreted in the urine. Titratable acids, such as phosphoric acid (choice E), make up a large fraction of the acids normally excreted in the urine. When stored fats are metabolized in large quantities, such as in diabetes mellitus, keto acids such as acetoacetic acid (choice C) make up a larger portion of the renal excreted titratable acids. Likewise, when the ischemic tissues pursue anaerobic metabolism, lactic acid (choice D) makes up a larger portion of the renal excreted titratable acids. Ammonia (choice A) is not a titratable cid, but it provides a mechanism for the kidney to excrete large amounts of acid during chronic metabolic acidosis.

QUESTION 146
Which of the following persons will have a negative free-water clearance?

A. one who begins excreting large volumes of urine with an osmolality of 100 mosm/kg H2O after severe head injury
B. one who drinks 2 L of distilled water in 30 minutes
C. one who is receiving lithium treatment for depression, and who develops polyuria that is unresponsive to administration ADH
D. one with an oat cell carcinoma of the lung, who excretes urine with an osmolality of 1000 mosm/kg H2O
E. one with neurogenic diabetes insipidus

Correct Answer: D
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
A negative free-water clearance occurs when the kidney is reabsorbing more water than it is excreting into the urine and is regulated by ADH. Choice D is correct because lung cancer can cause exogenous production of ADH, which will stimulate increased renal water reabsorption and thus a negative freewater clearance. Choice A is incorrect because the decreased ADH secretion that may occur following a severe head injury will result in a positive free-water clearance. Choice B is incorrect because rapid intake of 2 L of water will inhibit ADH secretion and thus trigger a positive free-water clearance. Choice C is incorrect because the insensitivity to ADH that occurs during lithium treatment will increase water excretion and thus cause a positive free-water clearance. Choice E is incorrect because a person with neurogenic diabetes insipidus has a reduced secretion of ADH, which will cause reduced renal water reabsorption and thus a positive free-water clearance.

QUESTION 147
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

Correct Answer: D
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
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.

QUESTION 148
A 40-year-old woman complains of chronic fatigue, aching muscles, and general weakness. Physical examination reveals a modest weight gain, dry skin, and slow reflexes. Laboratory findings include TSH: >10 mU/L (normal range 0.55 mU/L), free T4: low to normal. With of the following is the most likely explanation?

A. hyperthyroidism due to autoimmune thyroid disease
B. hyperthyroidism due to iodine excess
C. hyperthyroidism secondary to a hypothalamic-pituitary defect
D. hypothyroidism due to autoimmune thyroid disease
E. hypothyroidism secondary to a hypothalamic-pituitary defect

Correct Answer: D
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
The described symptoms are typical for hypothyroidism. Aprimary thyroid gland deficiency leads to low T4 levels and high TSH levels. The most common cause of thyroid gland failure is called autoimmune thyroiditis or Hashimoto thyroiditis. It develops slowly due to persistent inflammation of the thyroid caused by the patient's own immune system. Middle-aged women are most commonly affected. The measurement of elevated TSH levels in blood is of high diagnostic value, since it helps determine even minor degrees of hypothyroidism. Correct diagnosis is critical because treatment usually continues for life, and stopping of the treatment and

reevaluating the original diagnosis is often difficult. Opposite to hypothyroidism, hyperthyroidism (choices A, B, and C) presents with symptoms such as weight loss, warm moist skin, nervousness, and trembling hands. Secondary hypothyroidism (choice E) is caused by reduced TSH levels due to hypothalamic or pituitary insufficiency.

QUESTION 149
Apatient presents with long-standing emphysema. Which of the following would you expect to see in this individual?

A. decreased physiological dead space
B. increased FEV1/FVC
C. increased FRC
D. increased FVC
E. increased lung elastic recoil

Correct Answer: C
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
Destruction of lung tissue is a hallmark of emphysema. Due to this loss of elastic tissue, lung elastic recoil is decreased. Decreased elastic recoil (not increased, choice E) shifts the mechanical balance point between chest wall and lung to a higher volume--FRC is, therefore, increased. The barrel chest is characteristic of emphysema. Destruction of alveolar walls impairs gas exchange, causing an increase in physiological dead space (choice A). Tissue loss also causes a loss of radial traction with an increase in airway resistance--FVC is decreased (choice D). Emphysema is one type of chronic obstructive pulmonary disease. A decrease in the FEV1/FVC is characteristic of an obstructive disease (choice B).

QUESTION 150
A patient with newly diagnosed schizophrenia is given chlorpromazine. It is a drug that has amongst other effects moderate anticholinergic activity. As a consequence, which of the following is an expected side effect of this medication?

A. bradycardia
B. decreased GI sphincter tone
C. dry mouth
D. emptying of urinary bladder
E. increased GI motility

Correct Answer: C
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
Chlorpromazine is an antipsychotic drug with anticholinergic action (i.e., it inhibits the effects of parasympathetic stimulation). Parasympathetic stimulation causes copious secretion by nasal, lacrimal, and parotid glands. Consequently, parasympathetic blockade is leading to a dry mouth. Parasympathetic fibers slow the heart rate and anticholinergic drugs cause tachycardia rather than bradycardia (choice A). Functions of the parasympathetic nervous system include decreasing GI sphincter tone, increasing GI motility, and increasing emptying of the rectum and urinary bladder. Parasympathetic blockade would thus cause increased GI sphincter tone (choice B), urinary retention (choice D), and decreased GI motility (choice E) leading to constipation.

QUESTION 151
A patient presents with fever (her core temperature equals 39℃, with normal core temperature equaling 3637.5℃) as well as an elevated white cell count. Which of the following statements is true regarding the patient's elevated core body temperature?

A. Bacterial toxins act directly on skeletal muscle to increase muscle contractile activity, therebygenerating heat and elevating core temperature.
B. Core body temperature now exceeds the hypothalamic set point temperature.
C. Increased core body temperature is due to increased heat production by leukocytes.
D. Increased prostaglandins have raised the hypothalamic set point temperature.
E. The patient will be sweating in an effort to further elevate core temperature.

Correct Answer: D
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
In fever, cytokines act to increase prostaglandin levels in the hypothalamus. By an undefined mechanism, prostaglandins increase the hypothalamic set point temperature. The body's heat- generating mechanisms are activated to increase core body temperature until it approaches the new set point. Core temperature will approach but not exceed the set point temperature (choice B). Sweating lowers core temperature (choice E). Though bacterial toxins can be important in the etiology of fever, they do not act directly to increase muscle heat production (choice A). Leukocytes generate cytokines, which act centrally to influence the hypothalamus (choice C). The cellular activity that is most important in heat generation is muscle contraction.

QUESTION 152
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

Correct Answer: A
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
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).

QUESTION 153
A 55-year-old male with a history of smoking presents with a chronic cough with expectoration. He exhibits dyspnea on exertion, has a stocky build, and shows some cyanosis. Which of the following receptors is involved in the cough reflex?

A. carotid body chemoreceptors
B. central chemoreceptors
C. irritant receptors
D. lung stretch receptors
E. muscle spindles

Correct Answer: C
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
Foreign agents react with pulmonary irritant receptors, which participate in the cough reflex. Carotid body and central chemoreceptors (choices A and B) supply sensory information on arterial blood gas (and C) composition and thus modulate respiratory rate. Stretch receptors in the lung (choice D)

O_2

provide afferent information on the depth of breathing and can also influence respiration. Information from peripheral muscle spindles (choice E) can also modulate ventilation and is probably very important in setting the level of increased ventilation seen in moderate physical activity.

QUESTION 154
Which of the following is an adaptive response to moving from sea level to higher elevation?

A. bronchial relaxation
B. decreased cardiac output
C. decreased circulating levels of EPO
D. decreased levels of 2,3-diphosphoglycerate (2,3-DPG) in erythrocytes
E. hyperventilation

Correct Answer: E
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
At high elevation the decreased atmospheric pressure means that there is less available . Decreased

O_2

arterial P is sensed by peripheral chemoreceptors with a resultant increase in ventilation.

O_2

Hyperventilation helps to bring alveolar and thus arterial levels back toward normal. In hypoxic

O_2

conditions, erythrocyte 2,3-DPG levels (choice D) increase. This causes the oxygen-hemoglobin dissociation curve to shift to the right--thereby delivering a greater fraction of hemoglobin bound

O_2

to the tissues. At high elevation EPO levels (choice C) increase because the kidneys sense low-tissue oxygenation and respond by releasing EPO into the circulation. This hormone stimulates erythrocyte production thereby increasing total blood hemoglobin levels, helping to offset the hypoxia. In low-

O_2

conditions slight bronchoconstriction (choice A) can occur This is an adaptive response to hypoxia, since it will decrease dead space volume. With decreased dead space volume, a greater fraction of each breath contributes to alveolar ventilation, with more delivered to the system. In hypoxic conditions

O_2

cardiac output (choice B) increases to deliver more blood.

QUESTION 155
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

Correct Answer: E
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
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.

QUESTION 156
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 below figure. Which of the following is most likely affected?

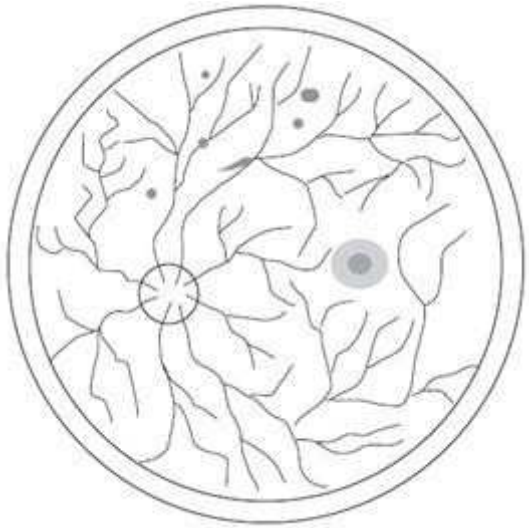


FIG. 2-15

A. color vision
B. high acuity vision
C. near point vision
D. scotopic vision
E. spatial vision

Correct Answer: D
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
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.

QUESTION 157
You are the primary care physician for a young female college student. She has been engaged over the past 3 months in a vigorous aerobic exercise training regime that includes a significant amount of running in a hot environment. You measure her hematocrit as part of a general physical examination. Her hematocrit could well be abnormal even though she is not anemic. Which of the following choices best fits this profile?

	Total circulating erythrocyte mass	Total plasma volume	Hematocrit
(A)	Decreased	Decreased	Decreased
(B)	Increased	Decreased	Decreased
(C)	Increased	Decreased	Increased
(D)	Unchanged	Decreased	Decreased
(E)	Unchanged	Increased	Decreased

A. Option A
B. Option B
C. Option C
D. Option D
E. Option E

Correct Answer: E
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
The central points of this question concern the definitions of hematocrit and anemia. Hematocrit is the proportion of blood that is packed cells. The hematocrit reading will be decreased by anything that lowers the number of cells, as well as by anything that increases the volume of plasma. Anemia refers to a condition in which the total circulating erythrocyte mass has decreased. In this student, a long-term regime of exercise in a warm environment has chronically increased her plasma volume, hence her hematocrit is low. However, since her total red blood cell mass is normal, there is no anemia. Choice E is correct. It is common to see a chronic increase in plasma volume develop in response to long-term exercise in a warm environment. Exercising in a warm environment places demands on the circulatory system, which must perfuse working muscles as well as skin capillary beds (to facilitate heat loss). In addition, volume is lost to sweating. Increased plasma volume helps the body meet these demands. In choice A, hematocrit could be low if erythrocyte mass decreased more than blood volume. However, this profile does not fit the question because this individual would be anemic, since erythrocyte mass is low. Choice B could not be correct since decreased plasma volume and increased red cell mass cause increased hematocrit. In choice C, the patient would not be anemic and hematocrit would be increased. However, this is not the best response since, as described above, in an individual exercising in a warm environment the hematocrit is often decreased and plasma volume is usually increased. In choice D, hematocrit would have to be increased.

QUESTION 158
A 66-year-old male presents with angina and dyspnea on exertion. Auscultation of the chest reveals a loud systolic murmur. He is diagnosed with aortic valvular sclerosis. This stenosis of the aortic valve will cause a murmur that can be heard loudest at which interval shown in below figure?

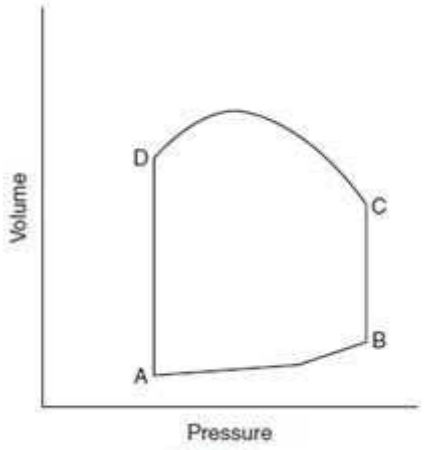


FIG. 2-16

A. between A and B
B. between B and C
C. between C and D
D. between D and A
E. between D and B

Correct Answer: C
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
Blood passes through the aortic valve, starting when the aortic valve opens at point C until it closes at point D. Hence aortic valve stenosis will cause turbulent blood flow (murmur) between C and D. Between Aand B (choice A) is the interval of diastolic filling when the aortic valve is closed. Between B and C is the period of isovolumetric contraction (choice B) before the aortic valve opens. Between D and Ais the period of isovolumetric relaxation (choice D) after the aortic valve closes. Between D and B the aortic valve is also closed.

QUESTION 159
Apatient is found to be deficient in folate. This patient is anemic, and a complete blood count indicates that the MCV is 105 fL (normal range: 8096) and the MCHC

is 34 g/dL (normal range: 3236). The anemia is thus macrocytic, normochromic. In this patient how would you predict that the MCH (mean corpuscular hemoglobin) would compare with the normal range?

A. MCH would be elevated with respect to the normal range
B. MCH would be depressed with respect to the normal range
C. MCH would be within the normal range
D. this cannot be determined based on the information provided

Correct Answer: A
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
These red blood cells are large (macrocytic) but have a normal hemoglobin concentration (normal MCH). Since MCH is mean hemoglobin content per red cell, this value must be elevated since the cells are large and the concentration in the cell is normal. Choice A excludes choices BD.

QUESTION 160
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

Correct Answer: C
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
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).

QUESTION 161
Which of the following conditions would likely be associated with decreased levels of circulating EPO?

A. chronic alkalosis
B. chronic renal failure
C. emphysema
D. pernicious anemia
E. pulmonary fibrosis

Correct Answer: B
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
EPO is a glycoprotein produced primarily in the kidney, thus EPO levels tend to be depressed in chronic renal failure. EPO is a growth factor that stimulates the production of red blood cells. Its production by the kidney is triggered by low tissue oxygenation. Any condition that decreases the oxygen-carrying capacity of the blood (such as anemia, choice D) or that causes hypoxia by decreasing lung function (such as emphysema or pulmonary fibrosis, choices C and E) will produce elevated levels of circulating EPO. Alkalosis (choice A) increases hemoglobin's affinity for oxygen, making it more difficult for tissues to extract oxygen from the blood. In alkalosis, tissues thus tend to have lower oxygen content, with a resultant increase in circulating EPO levels.

QUESTION 162
Exhibit:

A. $0.5\ cm\ H_2O/L$
B. $1\ cm\ H_2O/L$
C. $400\ mL/cm\ H_2O$
D. $800\ mL/cm\ H_2O$
E. $1000\ mL/cm\ H_2O$

The graph in below figure shows the static pressurevolume curve of a patient's lung (solid line). The broken line indicates the pressurevolume curve of a normal person for comparison. What is the approximate lung compliance of this patient over the volume range from 1 to 7 L?

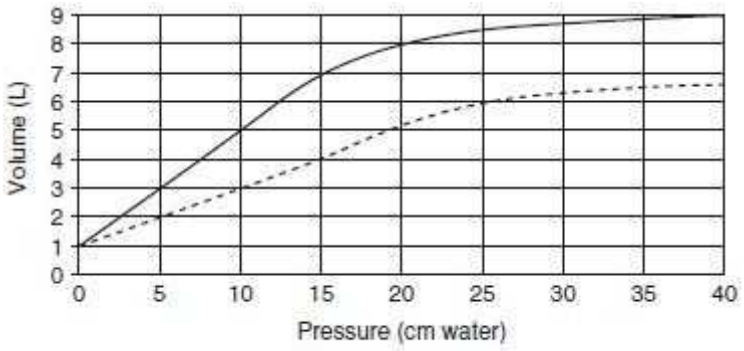


FIG. 2-17

A. A
B. B
C. C
D. D
E. E

Correct Answer: C
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
Compliance of the lung is the change in lung volume divided by the change in airway pressure (V/P). This patient's lungs have a compliance of 4 L/10 cm O = 400 mL/cm O. Lung

H_2

elasticity (choices A and B) is the inverse of compliance, and this patient's lungs have an elasticity of 1.25 cm O/L.

H_2

QUESTION 163
Exhibit #1:
Missing
Exhibit #2:

A. acute obstruction of the glottis
B. α_1-antitrypsin deficiency
C. asbestosis
D. idiopathic pulmonary fibrosis
E. sarcoidosis

The data in below figure indicate that the lung compliance in this patient (solid line) is altered relative to the norm. This patient is most likely suffering from which of the following conditions?

A. A
B. B
C. C
D. D
E. E

Correct Answer: B
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
Normal lung compliance is about and this patient's lung compliance is significantly

$0.2\ \mathrm{L/cm\ H_2O}$

higher than normal. High lung compliance occurs in -antitrypsin deficiency. Acute obstruction of

α_1

the glottis (choice A) does not affect lung compliance. Asbestosis (choice C), sarcoidosis (choice E), and idiopathic pulmonary fibrosis (choice D) are diseases that show a restrictive pattern and would have a compliance less than normal

$(< 0.2\ L/cm\ \mathrm{H_2O}).$

QUESTION 164
Lambert-Eaton myasthenic syndrome (LEMS) is an autoimmune disorder in which autoantibodies attack voltage-gated calcium channels in the presynaptic nerve

terminal. A characteristic 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

Correct Answer: D
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
At the neuromuscular junction, an invading action potential opens voltage-gated calcium channels and enters the presynaptic terminal. Elevated cytoplasmic causes release of vesicles

Ca^{2+}

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 enters the terminal of the presynaptic membrane--therefore less

Ca^{2+}

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 A and B). The MEPP is 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).

QUESTION 165
A newlywed 23-year-old woman and her 28-year-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)

Correct Answer: E
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
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 A and 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 granulose 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.

QUESTION 166
The electrocardiogram of a 66-year-old male with a history of atherosclerotic heart disease reveals an irregular, but rapid heart rate. The QRS complexes are normal but no P-waves can be seen. What is the most likely reason for these findings?

A. atrial fibrillation
B. Paroxysmal ventricular tachycardia
C. Right bundle branch block
D. Sinus tachycardia
E. Wolff-Parkinson-White syndrome

Correct Answer: A
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
Atrial fibrillation is a continuous, chaotic reentry of electrical impulses within the atrial myocardium that arises in a diseased or stretched left atrium. The chaotic patterns of atrial excitation prevent P- waves from being seen in the electrocardiogram. The ventricular response is rapid and irregular. In all the other alternatives (choices BE), a P-wave should be distinguishable in some part of the electrocardiogram, although not necessary in a constant relationship to the QRS complex.

QUESTION 167
Which of the following diseases will result in left ventricular hypertrophy?

A. Aortic valve stenosis
B. mitral valve stenosis

C. pulmonary valve regurgitation
D. tricuspid valve regurgitation
E. tricuspid valve stenosis

Correct Answer: A
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
Stenosis of the outlet valve of the left ventricle greatly increases the work of the ventricle in ejecting blood and will result in left ventricular hypertrophy. Mitral valve stenosis (choice B) will impede filling of the left ventricle and will not cause left ventricular hypertrophy. Tricuspid valve regurgitation (choice D), pulmonary valve regurgitation (choice C), and tricuspid valve stenosis (choice E) cause congestion of the right atria and/or right ventricles and impede flow of blood toward the left ventricle and thus will not result in left ventricular hypertrophy.

QUESTION 168
A 28-year-old, 166 cm (5.45 ft) tall woman, weighing 170 kg (375 lbs) successfully underwent biliopancreatic diversion surgery, in which a portion of her stomach was removed and the remaining portion of the stomach was connected to the lower portion of the small intestine (see below figure). What is her prevalence for peptic ulcer disease and for what reason?

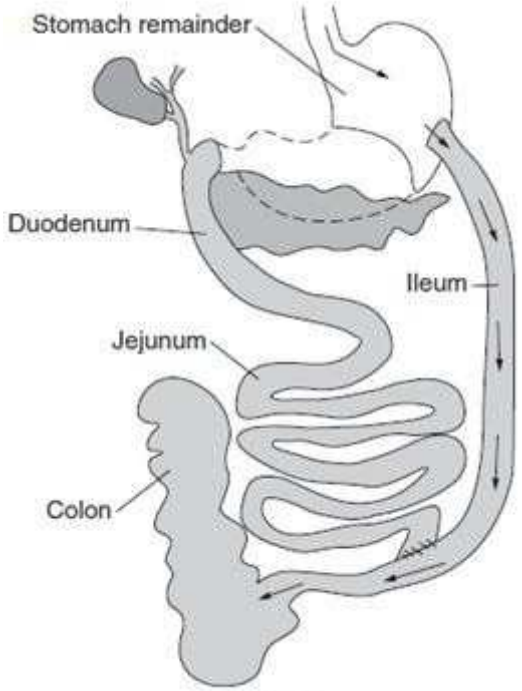


FIG. 2-18

A. it is higher due to inflammation caused by the surgical staples
B. it is higher due to the loss of secretin release
C. it is lower since chief cells were surgically resected
D. it is lower since G cells were surgically resected
E. it is unchanged since the surgery was successful

Correct Answer: D
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
Peptic ulcers refer to areas of the stomach or duodenal lining which became eroded by stomach acid. Stomach acid is produced by parietal cells which are stimulated by gastrin. Since gastrin-secreting G cells are primarily found in the gastric glands of the distal stomach (gastric antrum), the surgically removed

stomach portion, the patient's prevalence for peptic ulcer disease is lower after the surgery, and not unchanged as stated in choice E. However, the surgery is a dramatic event and increases the risk for many GI problems, including symptoms resulting from nutritional deficiencies. Hence, the surgery is only used for morbidly obese people (the patient's body mass index is above 50), who had no success with diet and medication. Inflammation potentially triggered by the surgical staples (choice A) might trigger prostaglandin release which has a protective function of the stomach lining. Although secretin (choice B) is known to suppress gastric acid release by inhibiting gastrin release, the lower number of G cells after surgery does not make this a good choice. Chief cells (choice C) are primarily present in the proximal stomach, the portion that remains after surgery.

QUESTION 169
In patients with type 4 renal tubular acidosis (RTA) aldosterone deficiency is often a prominent finding. Distal tubular transport of which of the following ions will be affected in these patients?

A. hydrogen and potassium in exchange for sodium
B. hydrogen only
C. potassium only
D. sodium and bicarbonate
E. sodium only

Correct Answer: A
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
The RTArefers to related conditions that are disorders of urine acidification even though other renal functions are not impaired. In type 4 RTA, distal nephron dysfunction is due to either inadequate aldosterone production or aldosterone resistance resulting from intrinsic renal disease. Thus, patients develop hyperchloremic acidosis with hyperkalemia, due to impaired distal tubular secretion of both potassium and hydrogen ions. Treatment of patients is directed at controlling serum potassium. Choices B, C, D, and E are inconsistent with the known actions of aldosterone.

QUESTION 170
A patient presented with an acute abdomen including fever, marked abdominal distension, acidosis, and leukocytosis. Laparoscopy revealed that large parts of the small intestine were necrotic and as a consequence, the entire ileum of the patient was resected. It is expected that very soon after the surgery the patient will have considerable problems resulting from the malabsorption of which of the following?

A. iron
B. bile acids
C. sodium
D. vitamin
E. protein

Correct Answer: B
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
After a meal about 90 percent of the bile acids and bile salts are absorbed from the lower ileum by way of active transport. They are directed to the liver, from where they can be released again via bile into the intestine. This enterohepatic circulation of bile acids between intestine and liver is physiologically very important for normal absorption of fat and fatsoluble vitamins, and if distorted, will lead to GI and other symptoms. The quantity of iron in the body (choice A) is maintained by controlled absorption from the duodenum, not the ileum. Although sodium (choice C) is actively absorbed in theileum, there are additional absorption mechanisms available in the jejunum and in the colon. For instance, in the jejunum, sodium is absorbed by cotransport coupled with sugars and neutral amino cids, and in the colon, there are active sodium transport mechanisms as well. Hence, no immediate sodium imbalance is expected. Although vitamin (choice D), complexed with intrinsic factor, binds to a

B_{12}

transmembrane receptor in the ileum for absorption, a large amount of vitamin (up to 5 mg) is

B_{12}

stored in the liver. This liver storage is thought to be sufficient for 36 years so that symptoms from vitamin deficiency will be expected at a later time, but not soon after removal of the ileum.

B_{12}

Protein digestion (choice E) occurs in the small intestine, with absorption of amino acids primarily in the jejunum and to a lesser extent in the ileum, and with dipeptide absorption at about equal rates in these two segments. Removal of the ileum will not immediately lead to problems due to protein malabsorption.

QUESTION 171
below figure shows a gastric parietal cell with selected membrane transporters and channels. What do X, Y, and Z represent in the figure?

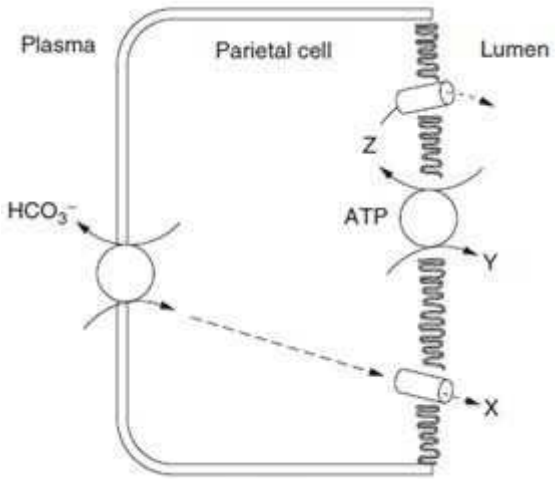


FIG. 2-22

	X	Y	Z
A.	Cl^-	H^+	K^+
B.	Cl^-	K^+	H^+
C.	H^+	Cl^-	HCO_3^-
D.	K^+	Na^+	H^+
E.	Na^+	H^+	K^+

A. Option A
B. Option B
C. Option C
D. Option D
E. Option E

Correct Answer: A
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
Parietal cells secrete an essentially isotonic solution of pure HCl containing 150 mM and 150 mM

Cl^-

into the gastric lumen. This is achieved by active transport of (Y) via / -ATPase in the

H^+

apical membrane that exchanges for (Z). Chloride ions are extruded passively down their

H^+

electrical gradient through --selective ion channels. They enter the cell via -

Cl^-

exchange that takes place at the basolateral membrane. The - comes from (the product

HCO_3

of carbonic anhydrase). None of the other choices reflect the correct ion distribution across the

$(B-E)$

gastric parietal cell.

QUESTION 172
Altered plasma renin levels can occur in both normal and pathologic conditions. Which of the following states is associated with a decrease in plasma renin levels?

A. heart failure
B. primary aldosteronism
C. renal artery stenosis
D. salt restriction
E. upright posture

Correct Answer: B

Section: Physiology
Explanation

Explanation/Reference:
Explanation:
Most patients with primary aldosteronism (Conn syndrome) have an adrenal adenoma. The increased plasma aldosterone concentration leads to increased renal Na+ reabsorption, which results in plasma volume expansion. The increase in plasma volume suppresses renin release from the juxtaglomerular apparatus and these patients usually have low plasma renin levels. Secondary aldosteronism is due to elevated renin levels and may be caused by heart failure (choice A) or renal artery stenosis (choice C). Salt restriction (choice D) and upright posture (choice E) decrease renal perfusion pressure and therefore increase renin release from the juxtaglomerular apparatus.

QUESTION 173
Exhibit #1:

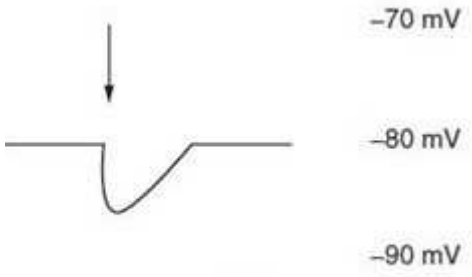


FIG. 2-23

Exhibit #2:

A. Ca^{2+}

B. Cl^{-}

C. K^{+}

D. Mg^{2+}

E. Na^{+}

Below figure 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 +, , +, , and are, respectively, +120 mV, +60 mV,

Ca^{2}

0 mV, -80 mV, and -90 mV. This neurotransmitter likely increases the conductance of which of the following ions?

A. A
B. B
C. C
D. D
E. E

Correct Answer: C
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
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 permeability would thus cause hyperpolarization, since its equilibrium

K^{+}

potential is negative with respect to the cell's resting membrane potential. Increased permeability (choices A, D, and E) would cause the cell membrane

$Ca^{2+}+, Na^{+}, or\ Mg^{2+}+$

potential to depolarize. Increased Cl_ permeability (choice B) would not alter the membrane's potential.

QUESTION 174
Below figure shows an intracellularly recorded action potential from a mammalian neuron. Which of the following statements is correct concerning events taking place at the point in time indicated by the arrow?

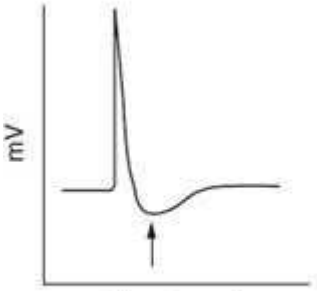


FIG. 2-24

A. calcium conductance is higher than its normal resting level
B. chloride conductance is higher than its normal resting level
C. potassium conductance is higher than its normal resting level
D. sodium conductance is higher than its normal resting level
E. sodium-potassium ATPase activity is depressed

Correct Answer: C
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
The neuron, at the arrow, is in the refractory period following the action potential. The membrane potential is more negative (hyperpolarized) than its normal resting level because potassium conductance is elevated. The after hyperpolarization is also due to the fact that sodium channels are inactivated causing lower than normal sodium conductance (choice D). In skeletal muscle neither calcium (choice A) nor chloride (choice B) conductances should be elevated. After the action potential, intracellular sodium concentration could be slightly elevated due to the sodium influx that occurred during the action potential. This could stimulate the Na, K-ATPase (choice E).

QUESTION 175
Heparin is a rapidly acting, potent anticoagulant that has many important clinical uses. Which of the following is an action of heparin?

A. activates prothrombin
B. acts with antithrombin to inhibit thrombin activity
C. decreases prothrombin time
D. inhibits calcium action
E. promotes vitamin K activity

Correct Answer: B
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
Thrombin is a critical enzyme in the coagulation cascade. It not only can activate factors VIII and V, it also acts on fibrinogen to form fibrin. Thrombin is essential for clot formation. Antithrombin III modulates the coagulation cascade, serving to inhibit thrombin activity. Heparin acts as an anticoagulant because it accelerates the action of antithrombin III. Heparin does not stimulate vitamin K activity (choice E) and, in any case, anything that promoted vitamin K activity would increase coaguability, since vitamin K is necessary for synthesis of multiple coagulation factors. Activation of prothrombin (choice A) promotes coagulation. Though calcium is an essential cofactor for coagulation, heparin does not act via calcium inhibition (choice D). Because heparin inhibits thrombin action, it would prolong prothrombin time (choice C).

QUESTION 176
Which of the following is a true statement regarding renal clearance of a substance?

A. is measured in milligram per minute
B. glucose is greater than that of insulin in the normal kidney
C. insulin is zero
D. PAH remains constant regardless of the plasma level
E. potassium clearance will increase after an injection of aldosterone

Correct Answer: E
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
Choice E is correct since the clearance of potassium is normally regulated by the action of aldosterone on the distal tubule exchange of sodium reabsorption with

potassium secretion. Choice Ais incorrect because renal clearance represents the volume of plasma completely cleared of a substance per unit time, hence the units for renal clearance are milliliter per minute, and not milligram per minute. Choice B is incorrect because a normal kidney reabsorbs 100% of the filtered glucose, so glucose clearance is zero. By contrast, a significant amount of inulin is usually cleared by the kidney. Choice C is incorrect because although inulin is not secreted by the tubule as is PAH, inulin is filtered but not reabsorbed and thus a normal kidney will clear approximately 20% of the inulin from the plasma. Choice D is incorrect because PAH is actively secreted by the proximal tubule. Above a certain plasma level, PAH secretion no longer can increase and thus clearance (calculated as the ratio of urine to plasma concentration multiplied by urine flow) will decline as plasma PAH concentration increases faster than urine PAH concentration.

QUESTION 177
As part of a neurological examination, a patient is placed in a chair that rotates to the right under the control of a computer so that the patient's head and body move in unison with the chair. How would a healthy person react immediately upon getting off the chair that turned for 1 minute?

A. behave the same as before the rotation
B. display post-rotational eye nystagmus to the right
C. experience a vertigo that would be diminished if he immediately got back in the rotating chair
D. experience "past pointing" to the left when asked to reach a target
E. fall to the left when asked to walk on a straight line

Correct Answer: C
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
For about 2030 seconds after the rotation stops, the endolymph of the vestibular system continues to rotate due to its inertia. The brain still receives the input of rotation, while the input from the person's eyes and mechanoreceptors signal that the motion stopped. This conflicting information causes dizziness which would disappear if the person continue rotating. The eyes of a healthy person would be "flicking" in the direction opposite to the direction of rotation, so that nystagmus would be to the left, not to the right (choice B). If the person attempts to reach out and touch a target during the postrotatory nystagmus, the movement will miss the target in the direction of the slow phase of nystagmus, to the right in this case, not to the left (choice D). An attempt to walk during the period of nystagmus and vertigo induced by ceasing rotation often leads to a fall, in this case to the right, not to the left (choice E). The compensatory movements to the right are due to the fact that the brain interprets the continuing rotation of the endolymph in relation to the now unmoving outer walls of the vestibular organs as if a rotation to the left has begun. This incorrect input signal is processed by the brain to influence eyes, trunk, and limb muscles to exert compensatory actions. The responses are entirely normal and their absence could indicate dysfunction of the peripheral or central vestibular system (choice A).

QUESTION 178
One of your diabetic patients has a blood glucose level of 200 mg/dL. Surprisingly, a dipstick test is negative for urinary glucose. How could this finding be explained?

A. dipstick tests are more sensitive for reducing sugars other than glucose
B. the patient has defective tubular glucose transporters

C. the patient has diabetes insipidus
D. the patient has significantly reduced GFR
E. the patient is in a state of antidiuresis

Correct Answer: D
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
Glucose excretion by the kidneys depends on the glomerular filtration and tubular reabsorption rates. Glucose first appears in the urine, when the capacity of the glucose transporters in the proximal tubuli cells is exceeded. This usually occurs at plasma glucose levels higher than 180 mg/dL. Patients with longstanding diabetes mellitus often have decreased renal function and reduced GFR. Under these circumstances the threshold (i.e., plasma level) for excretion of glucose is higher than in a healthy person. Urine dipsticks nowadays are both sensitive and specific for glucose, detecting as little as 100 mg/dL (choice A). Earlier dipstick tests were sensitive but not specific (they detected other reducing sugars in addition to glucose). Adefect in glucose transporters (choice B) results in glucosuria even at normal plasma glucose concentration. Patients with diabetes insipidus (choice C) have a large urine output due to absence of ADH or defective renal ADH receptors, but should not have a plasma glucose level of 200 mg/dL. Antidiuresis (choice E) increases the concentration of solutes in the urine and increases the sensitivity to detect urine glucose. Reabsorption of filtered glucose occurs in the proximal tubule by active transport.

QUESTION 179
Exhibit:

A. normally generates a lumen-positive transepithelial potential difference
B. normally reabsorbs potassium and secretes sodium
C. responds to aldosterone with increased water permeability via aquaporins
D. utilizes a Na^+/K^+ -ATPase in the basolateral cell membrane
E. utilizes a $Na^+/K^+/2C1^-$ cotransport protein in the luminal cell membrane

Please refer to the exhibit:
Which of the following is a feature of the principal cell in the cortical collecting duct?

A. A
B. B
C. C
D. D
E. E

Correct Answer: D
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
The principal cell is the major sodiumreabsorbing and potassium-secreting cell in the collecting duct. It functions via specific sodium and potassium channels that increase luminal cell membrane permeabilty to these ions and a sodium/potassium ATPase in the basolateral cell membrane. Choice A is incorrect because the specific movement of sodium through the luminal membrane via specific sodium channels creates an excess of negative charges in the tubular lumen. Choice B is incorrect because sodium is reabsorbed while potassium is predominantly secreted by this cell. Choice C is incorrect because aldosterone regulates sodium and potassium transport, not water transport. ADHdoes increase water transport via aquaporins. Choice E is incorrect because a sodium/potassium/2 chloride transporter is not located in this cell type, but is located in the thick ascending loop of Henle cells instead.

QUESTION 180
Which of the following shows the correct effects of hormones, when increased in serum, on liver glycogen content?

	Catecholamines	Glucocorticoids	Glucagon
(A)	Decreased	Decreased	Decreased
(B)	Decreased	Decreased	Increased
(C)	Decreased	Increased	Decreased
(D)	Increased	Decreased	Increased
(E)	Increased	Increased	Decreased

A. A
B. B
C. C
D. D
E. E

Correct Answer: C
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
Glucagon and catecholamines such as epinephrine stimulate the mobilization of glycogen by triggering the cAMP cascade. Hormones that increase liver cell cAMP promote glycogen breakdown, and hormones that decrease liver cell cAMP promote glycogen synthesis. Cortisol, the main glucocorticoid, regulates the

metabolism of proteins, fats, and carbohydrates. It acts on most organs catabolically. However, on the liver it has anabolic effects, increasing glycogen synthesis and accumulation in the liver. Choices A, B, D, and E do not correctly reflect the effects of the three different agents on glycogen metabolism.

QUESTION 181
Opioid peptides are an important physiological mechanism of the body for relief from painful stimuli. Used as pharmacologic agents, they are highly valuable tools for pain management, although side effects are usually inevitable. Which of the following problems are most likely during opiate treatments?

A. difficulty sleeping
B. hypermotility of the GI tract
C. placebo effects
D. respiratory alkalosis
E. tolerance (need for higher dosage to achieve the same therapeutic effect)

Correct Answer: E
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
Tolerance is commonly observed with many pharmacologic agents, including opioids. Difficulty sleeping (choice A), hypermotility of the GI tract (choice B), and respiratory alkalosis (choice D) are opposite to the expected effect of opiates. The placebo effect (choice C) is, at least in part, likely due to the release of endogenous opioid peptides in anticipation of pain relief, but is not a complication or side effect of therapy.

QUESTION 182
Following an automobile accident a patient suffers a pelvic fracture and significant internal blood loss resulting in hemorrhagic shock. Which of the following organs has the largest specific blood flow (blood flow per gram of tissue) under resting conditions and is especially vulnerable during the shock phase?

A. brain
B. heart muscle
C. kidneys
D. skeletal muscle
E. skin

Correct Answer: C
Section: Physiology
Explanation

Explanation/Reference:
Explanation:

During resting conditions, approximately 15% of the cardiac output goes to the brain, 15% to the muscles, 30% to the GI tract, and 20% to the kidneys. However, when normalized by organ weight, the kidneys receive the largest specific blood flow (400 mL/100 g) at rest and are particularly vulnerable during hemorrhagic shock. The brain (choice A) also receives relatively high specific blood flow (50 mL/100 g). Heart muscle (choice B), not surprisingly, also has a relatively high resting specific blood flow (60 mL/100 g), which may increase fivefold during exercise. Skeletal muscles (choice D) have low specific blood flow (23 mL/100 g) at rest, which may increase up to 20-fold during strenuous exercise. Blood flow through the skin (choice E) varies between 1 and 100 ml/100 g and serves temperature regulation.

QUESTION 183
A 75-year-old male presented with a 6-month history of early satiety and with upper abdominal discomfort for many years. Physical examination revealed mild epigastric tenderness. Esophago-gastro- duodenoscopy showed a large, ulcerated mass in the upper stomach, which was found to be cancerous. Surgery resulting in the removal of the gastric fundus was performed. After successful surgery, the patient was advised to eat small portions and to drink small volumes because of which of the following?

A. almost complete absence of gastric motility
B. distorted emptying of liquids
C. inadequate mixing of large food boluses
D. lack of receptive relaxation in the stomach
E. weaker and slower propulsion of food toward the pylorus

Correct Answer: D
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
The receptive relaxation reflex is a feature of the orad stomach, composed of the fundus and upper stomach body. Without food, the orad stomach shows low frequency, sustained contractions that are responsible for generating a basal pressure within the stomach. When food enters the stomach, a reflex is initiated, which allows gastric accommodation of large increases in volume with only small increases in intragastric pressure. The tonic contractions of the orad stomach also contribute to some extent to gastric emptying (choice B), since they generate a pressure gradient from the stomach to the intestine. However, neural and hormonal components play a more important role in regulating gastric emptying, which makes this not the best choice. Since the lower stomach is not affected by the surgery, characteristic motility patterns of the distal stomach remain (choice A). Features of the distal stomach include strong peristaltic waves of contractions, which cause the mixing of the chyme with digestive secretions (choice C), the grinding of the particles to a small size, and the propulsion through the gastroduodenal junction (choice E). All these motility patterns would still be a feature of the remaining stomach.

QUESTION 184
A 68-year-old woman presents with sleep disturbances and memory loss. After careful analysis, she is diagnosed with early stages of Alzheimer's disease. Her pharmacological treatment plan includes acetylcholine esterase inhibitors. One week after starting treatment, the woman's daughter calls in, reporting that her mom has developed new symptoms that might be related to her new medicine. Which of the following is a likely side effect of the drug?

A. dry mouth

B. forgetting to urinate
C. muscle weakness
D. nausea and diarrhea
E. vertigo

Correct Answer: D
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
Increasing the lifetime of acetylcholine by inhibiting its enzymatic breakdown might help existing brain cells to work better. Studies found that Alzheimer patients at early stages might benefit from cholinergic therapy by small improvements in cognitive abilities and a delay in the progression of the disease. However, the side effects of acetylcholine therapy may outweigh the benefits of it. The increased concentration of acetylcholine at postsynaptic nerve endings of the parasympathetic nervous system can result in excessive stimulation of peripheral organ muscarinic and nicotinic receptors. Increased GI motility may occur resulting in nausea and diarrhea. For the same reason, increased salivation, not decreased as in choice A, and increased micturition, and not decreased as in choice B, are expected. Less common side effects include muscle cramps, not muscle weakness as in choice C, due to overstimulation of the cholinergic neuromuscular junction. Acetylcholine overdosing for an extensive time might eventually lead to muscle weakness due to desensitization of postsynaptic acetylcholine receptors, but this is not the best choice in this case. Vertigo (choice E) is the sensation that the room is spinning. Although neurological problems can always lead to kinetoses, there is no direct connection between acetylcholine esterase inhibitors and vertigo.

QUESTION 185
A 14-year-old female presenting with polyuria is subsequently diagnosed with Type I diabetes mellitus. The polyuria results from an osmotic diuresis that involves primarily which part of the renal tubule?

A. collecting duct
B. glomerulus
C. juxtaglomerular apparatus
D. proximal tubule
E. thick ascending limb of the loop of Henle

Correct Answer: D
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
The proximal tubule reabsorbs the majority (about two-thirds) of filtered salt and water. Both the luminal salt concentration and the luminal osmolality remain constant (and equal to plasma values) along the entire length of the proximal tubule. Water and salt are reabsorbed proportionally because the water is dependent on and coupled with the active reabsorption of Na+. The water permeability of the proximal tubule is high, and therefore a significant transepithelial osmotic

gradient is not possible. Sodium is actively transported, mainly by basolateral sodium pumps, into the lateral intercellular spaces; water follows. Increased glucose filtration in diabetes will osmotically prevent water reabsorption at this site. The collecting duct (choice A) reabsorbs only a small fraction of filtered Na+ and has a variable water permeability (dependent on ADH levels). The glomerulus (choice B) is where solutes are filtered from the plasma, no reabsorption of salt and water occurs here. The juxtaglomerular apparatus (choice C) produces renin. The thick ascending limb of the loop of Henle (choice E) actively transports and from lumen to the peritubular space using a cotransporter,

Na^+

but is water impermeable so osmotic diuresis will not be produced here.

QUESTION 186
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

Correct Answer: C
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
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 A is 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.

QUESTION 187
With respect to below figure, which of the following will decrease the GFR?

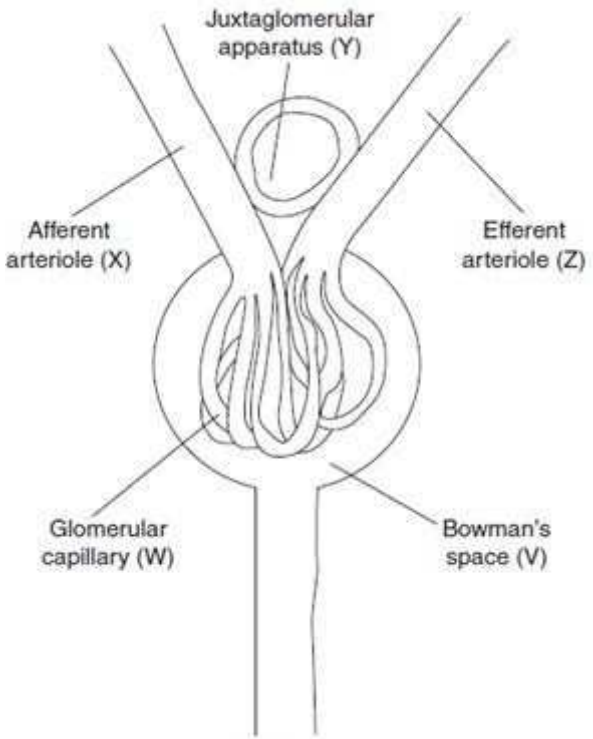


FIG. 2-27

A. decreased hydrostatic pressure in V
B. decreased plasma protein concentration in W
C. dilation of X
D. dilation of Z
E. increased aldosterone secretion by Y

Correct Answer: D
Section: Physiology
Explanation

Explanation/Reference:
Explanation:

These choices revolve around the Starling forces that directly regulate glomerular filtration. Choice D is correct and choice C is incorrect because glomerular capillary pressure is regulated by the ratio of upstream (afferent arteriole) and downstream (efferent arteriole) resistance to flow. Dilation of the afferent arteriole (choice C) will increase glomerular capillary pressure and increase filtration, whereas dilation of the efferent arteriole (choice D) will decrease the pressure and thus decrease filtration. Choice A is incorrect because Bowman's space pressure normally acts to oppose filtration, hence a decreased pressure will increase filtration. Choice B is incorrect because the osmotic pressure of the plasma proteins opposes filtration, so a decreased plasma protein concentration will predictably increase filtration. Choice E is incorrect, first of all because the juxtaglomerular apparatus does not secrete aldosterone, but instead secretes renin, which ultimately can trigger aldosterone secretion from the adrenal cortex via angiotensin II. Secondly, aldosterone is likely to trigger salt and water retention by an action on the distal nephron of the kidney, which is likely to alter the Starling forces in favor of increased glomerular filtration.

QUESTION 188
Exhibit:

A. calcium-ATPase
B. GLUT2
C. Na^+, K^+-ATPase
D. Na^+: Ca^{2+} countertransport protein
E. SGLT-1

Please refer to the exhibit.
Which of the following proteins uses the sodium electrochemical gradient to actively transport a solute into the cell?

A. A
B. B
C. C
D. D
E. E

Correct Answer: E
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
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.

QUESTION 189
A 23-year-old female has serum electrolytes tested as part of a routine physical. The laboratory results reveal a mild degree of hypokalemia. Which of the following will promote movement of extracellular potassium into the intracellular fluid compartment and cause hypokalemia?

A. extracellular fluid hyperosmolality
B. intravenous administration of a betaadrenergic blocker
C. intravenous administration of insulin
D. metabolic acidosis
E. physical exercise

Correct Answer: C
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
Among other actions, insulin is known to stimulate the uptake of potassium into cells of the body via stimulation of the , ATPase. Choices and will either have the opposite action, or

Na^+

no effect.

QUESTION 190
Below figure shows blood glucose levels after ingestion, at the arrow of 100 grams of glucose in a patient newly diagnosed with Type II diabetes. The curve labeled R is the patient's reference response. After curve R was obtained, the patient commenced a daily exercise regime. After several weeks of exercise a second curve was obtained. Which of the following best describes the response to glucose after exercise training?

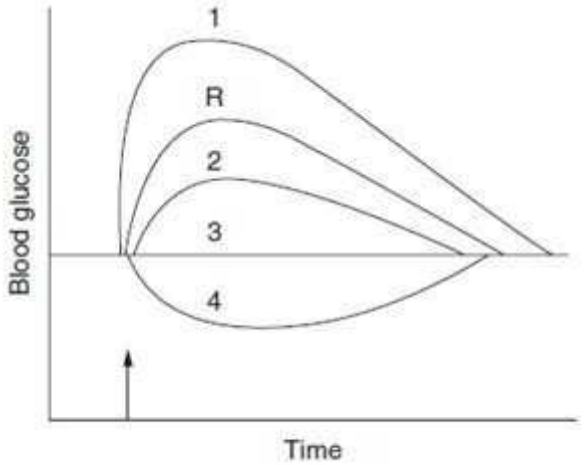


FIG. 2-28

A. curve 1
B. curve 2
C. curve 3
D. curve 4

Correct Answer: B
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
Exercise recruits both non-insulin-dependent and insulin-dependent glucose transport proteins to the plasma membrane of active skeletal muscle cells. This effectively increases sensitivity to insulin and the response to ingested glucose is blunted after exercise training. This excludes choice E, which states that no effect can be expected from exercise and choice A (curve 1), which represents a state of lower insulin receptor sensitivity compared to the sedentary state R. Ingestion of glucose will cause an initial rise of blood glucose in both active and sedentary people (excludes choices C and D).

QUESTION 191
A deficiency of argininosuccinate synthetase (ASD) can be suspected in a 2448-hour-old neonate with elevated serum ammonia. To discriminate the fact that the hyperammonemia is indeed due to ASD and not due to a deficiency in other urea cycle enzymes, one can assay for the serum concentration of citrulline and urinary orotic acid concentration. Which of the following would best describe the expected findings?

A. Both citrulline and orotate levels will be low.
B. Citrulline levels will be absent but orotate will be elevated.
C. Citrulline levels will be between 100300 M and orotate levels will be elevated.
D. Citrulline levels will be >1000 M, orotate will be near normal.

Correct Answer: D
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
A urea cycle disorder (UCD) is likely in a neonate that has elevated serum ammonia appearing, not before, but between 24 and 48 hours after a normal term delivery. There are three hallmark symptoms associated with UCDs. These are hyperammonemia, encephalopathy, and respiratory alkalosis. Thus, elevated serum ammonia is not, in and of itself, indicative of a specific defect in the urea cycle. An analysis of the levels of various amino and organic acids in the plasma and urine is the primary key to determining which defect led to the elevation in serum ammonia. Differential diagnosis of neonatal hyperammonemia, as a consequence of a UCD can be accomplished by measurement of plasma citrulline and urinary orotic acid levels. Shown in below figure is the standard differential diagnosis chart for determining which of four possible neonatal UCDs is the cause of the hyperammonemia.

First, the hyperammonemia appears in the absence of any significant acidosis or ketosis. If analysis of serum citrulline demonstrates that it is >1000 M it is confirmation that the clinical symptoms are due to a deficiency in ASD. In this circumstance it is not necessary to assay for levels of urinary orotic acid but they would be expected to be normal. Since citrulline levels are dramatically elevated in cases of ASD, choices A, B, and C are not correct.

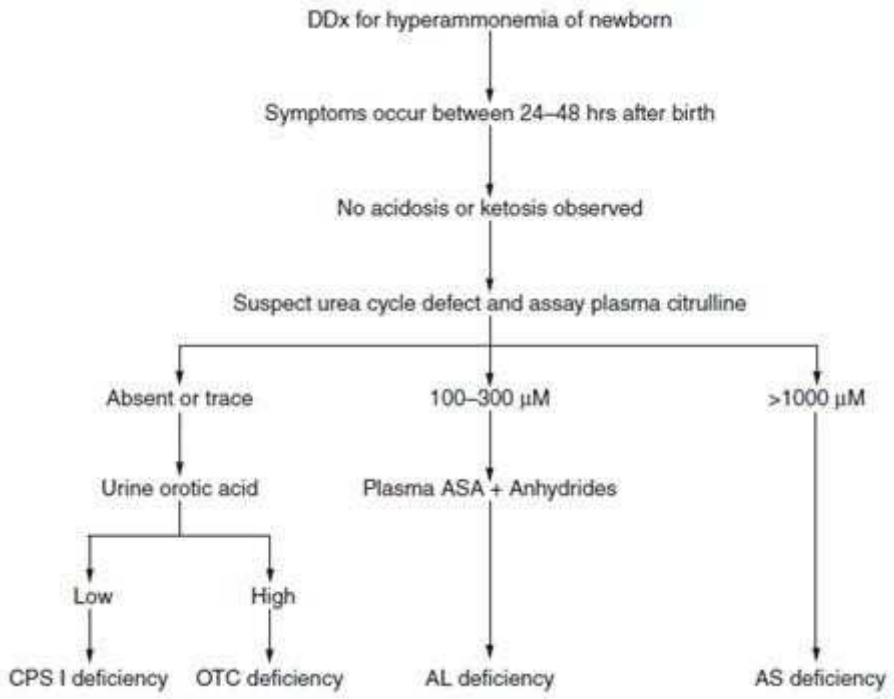


FIG. 3-6

QUESTION 192
A 7-year-old boy is examined by his pediatrician because of complaints of severe cramping pain in his legs whenever he rides his bike. He also expriences nausea and vomiting during these attacks. The child has noted that the severity of the cramps is most intense after dinners that include baked potatoes or pasta, and sometimes bread. Clinical studies undertaken following a treadmill test demonstrate myoglobinuria, hyperuricemia, and increased serum bilirubin. Which of the following enzyme deficiencies is associated with these clinical findings?

A. glucose-6-phosphatase
B. glycogen synthase
C. liver glycogen debranching enzyme
D. muscle phosphofructokinase
E. muscle phosphorylase

Correct Answer: D
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
A deficiency in muscle phosphofructokinase results in glycogen storage disease type VII (Tarui disease). Clinically, the symptoms seen in Tarui disease are very similar to those seen in muscle phosphorylase deficiency (choice E), glycogen storage disease type V (McArdle disease) such as exercise-induced cramping and early fatigue. There are five clinical characteristics allowing distinction between Tarui and McArdle diseases: exercise intolerance is evident in childhood, is more severe, and is associated with nausea and vomiting; the intolerance is particularly acute following meals rich in carbohydrates; hyperuricemia is more severe; compensated hemolytic anemia is evidenced by increased serum bilirubin and reticulocyte count, and lastly; an abnormal polysaccharide is present in muscle fibers. Deficiency in glucose-6-phosphatase (choice A) is one cause of glycogen storage disease type I (specifically type Ia, von Gierke disease). Classic symptoms of this deficiency include neonatal hypoglycemia and lactic acidosis. If symptoms do not appear until the third or fourth month they include hepatomegaly and hypoglycemic seizures. Liver glycogen synthase deficiency (choice B) presents with morning fatigue and ketotic hypoglycemia on fasting--both of which rapidly disappear on feeding. Symptoms can be rapidly relieved and chemical signs corrected by introducing frequent protein-rich meals and nighttime feedings of suspensions of uncooked corn starch. Deficiency in glycogen debranching enzyme (choice C) results in glycogen storage disease type III (Cori or Forbes disease). Symptoms of type III disease are short stature, variable skeletal myopathy, cardiomyopathy, hepatomegaly, and hypoglycemia.

QUESTION 193
An adult man suffered from stable angina pectoris for 15 years, during which time there was progressive heart failure and repeated pulmonary thromboembolism. On his death at age 63, autopsy disclosed enormous cardiomyopathy (1100 g), cardiac storage of globotriaosylceramide (11 mg lipid/g wet weight), and restricted cardiocytes. Which of the following lipid storage diseases would result in these clinical findings?

A. Fabry disease
B. Gaucher disease
C. Krabbe disease
D. Niemann-Pick disease (NPD) type I A
E. Tay-Sachs disease

Correct Answer: A
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Fabry disease is an X-linked disorder that results from a deficiency in alpha-galactosidase A. This leads to the deposition of neutral glycosphingolipids with terminal alpha-galactosyl moieties in most tissues and fluids. Most affected tissues are heart, kidneys, and eyes. The predominant glycosphingolipid accumulated is globotriaosylceramide [galactosyl-(14)- galactosyl-(14)-glucosyl-(11')-cer amide]. With increasing age, the major symptoms of the disease are due to increase in deposition of glycosphingolipid in the cardiovascular system. Indeed, cardiac disease occurs in most hemizygous males. Three types of Gaucher disease (choice B) have been characterized and are caused by defects in lysosomal acid beta-glucosidase (glucocerebrosidase). Defects in this enzyme lead to the accumulation of glucosylceramides (glucocerebrosides), which leads, primarily, to central nervous system (CNS) dysfunction and also hepatosplenomegaly and skeletal lesions. NPD (choice D) comprises three types of lipid storage disorder, two of which (type A and B NPD) result from a defect in acid sphingomyelinase. Type A is a disorder that leads to infantile mortality. Type B is variable in phenotype and is diagnosed by the presence of hepatosplenomegaly in childhood and progressive pulmonary infiltration. Pathologic characteristics of NPD are the accumulation of histiocytic cells that result from phingomyelin deposition in cells of the monocyte-

macrophage system. Tay-Sachs disease (choice E) results from a defect in hexosaminidase A leading to the accumulation of

GM_2

gangliosides, particularly in neuronal cells. This defect leads to severe mental retardation, progressive weakness, and hypotonia, which prevents normal motor development. Progression of the disease is rapid and death occurs within the second year. Krabbe disease (choice C), also called globoid-cell leukodystrophy, results from a deficiency in galactosylceramidase (galactocerebroside betagalactosidase). This disease progresses rapidly and invariably leads to infantile mortality.

QUESTION 194
An investigational diabetes treatment involving a hypoglycemia-inducing drug has been developed. This drug is designed to inhibit dipeptidylpeptidase IV (DPP IV) activity and has been shown to decrease plasma glucose concentration and pancreatic glucagon secretion. DPP IV hydrolyzes which of the following hormones such that its inhibition results in the observed effects?

A. glucagon
B. glucagon-like peptide-1 (GLP-1)
C. insulin
D. insulin-like growth factor-I (IGF-I)
E. pancreatic polypeptide

Correct Answer: B
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
GLP-1 is derived from the product of the proglucagon gene. This gene encodes a preproprotein that is differentially cleaved depending on the tissue in which it is synthesized. In the gut, prohormone convertase 1/3 action leads to release of several peptides including GLP-1. On nutrient ingestion GLP- 1 is secreted from intestinal enteroendocrine Lcells. Bioactive GLP-1 consists of two forms: GLP-1(7-
37) and GLP-1(7-36) amide, where the latter form constitutes the majority (80%) of the circulating hormone. The primary physiologic responses to GLP-1 are glucose-dependent insulin secretion, inhibition of glucagon secretion, and inhibition of gastric acid secretion and gastric emptying. The latter effect will lead to increased satiety with reduced food intake along with a reduced desire to ingest food. The action of GLP-1 at the level of insulin and glucagon secretion results in significant reduction in circulating levels of glucose following nutrient intake. The glucose-lowering activity of GLP-1 is highly transient as the halflife of this hormone in the circulation is less than 2 minutes. Removal of bioactive GLP-1 is a consequence of N-terminal proteolysis catalyzed by DPP IV. DPP IV is also known as the lymphocyte surface antigen CD26 and has numerous activities unrelated to hormone inactivation. Although targeting compounds that can inhibit the enzymatic action of DPP IV would seem like ideal candidates for treating the hyperglycemia of uncontrolled diabetes, there are several unknowns associated with DPP IV inhibition. One of these issues is the fact that GLP-1 is only one of the many known substrates for DPP IV cleavage. Thus, prolonged inhibition of DPP IV enzymatic activity may have unexpected consequences unrelated to control of hyperglycemia. DPP IV is not known to hydrolyze glucagons (choice A), insulin (choice C), IGF-I (choice D), nor pancreatic polypeptide (choice E).

QUESTION 195
A 25-year-old man has experienced chronic blistering and scarring of his skin when exposed to sunlight. This man is a smoker and drinks heavily, both of which exacerbate his responses to sunlight. Analysis of his urine and plasma indicates a high accumulation of complex porphyrins, predominantly uroporphyrin. The symptoms and clinical signs displayed by this patient indicate he is suffering from which of the following disorders?

A. acute intermittent porphyria (AIP)
B. hereditary coproporphyria (HCP)
C. porphyria cutanea tarda (PCT)
D. variegate porphyria
E. X-linked sideroblastic anemia

Correct Answer: C
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
PCT is the most common porphyria. Symptoms of PCT include cutaneous involvement and liver abnormalities, cutaneous features include chronic blistering lesions on sun-exposed skin. These lesions lead to skin thickening, scarring, and calcification. Symptoms usually develop in adults and are exacerbated by excess hepatic iron, alcohol consumption, induction of cytochrome enzymes as

P_{450}

occurs in smokers. Symptoms of AIP (choice A) usually appear after puberty and are more frequent in females than in males. The majority of AIP carriers (>80%) do not exhibit symptoms, those who do manifest intermittent neurologic complications with no cutaneous photosensitivity. HCP (choice B) has clinical features and precipitating factors that are essentially identical to those of AIP with the addition of occasional skin photosensitivity. Veriegate porphyria, VP (choice D), symptoms are also very similar to those of AIP and HCP, but photosensitivity is more common than in HCP. X-linked sideroblastic anemia (choice E) is due to a defect in erythoid-specific porphyrin synthesis. The reduction in heme synthesis in affected individuals leads to erythropoiesis, which is ineffective. This results in nonferritin iron accumulation in the mitochondria of erythroblasts giving rise to the characteristic ring sideroblasts.

QUESTION 196
A 4-month-old boy presents with painful progressive joint deformity (particularly the ankles, knees, elbows, and wrists), hoarse crying, and granulomatous lesions of the epiglottis and larynx leading to feeding and breathing difficulty. Biopsy of the liver indicates an accumulation of ceramides. The observed symptoms and the results of the liver biopsy are indicative of which disease?

A. Farber lipogranulomatosis
B. fucosidosis
C. Gaucher disease
D. metachromic leukodystrophy

E. Sandhoff-Jatzkewitz disease

Correct Answer: A
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Farber lipogranulomatosis is characterized by painful and progressively deformed joints and progressive hoarseness due to involvement of the larynx. Subcutaneous nodules form near the joints and over pressure points. Granulomatous lesions form in these tissues and there is an accumulation of lipid-laden macrophages. Significant accumulation of ceramide and gangliosides is observed, particularly in the liver. If these compounds accumulate in nervous tissue there may be moderate nervous dysfunction. The illness often leads to death within the first few years of life, although milder forms of the disease have been identified. Fucosidosis (choice B) is characterized by the accumulation and excretion of glycoproteins, glycolipids, and oligosaccharides- containing fucoside moieties. Symptoms of fucosidosis include psychomotor retardation, dystosis multiplex (a term referring to multiple skeletal abnormalities), growth retardation, and coarse facial features. Gaucher disease (choice C) is characterized by an accumulation of glucosylceramide (glucocerebroside). Several forms of the disease have been identified and vary in severity. Typical symptoms include hepatosplenomegaly, bone lesions, and CNS involvement. Occasionally, the lungs and other organs may be involved. Metachromic leukodystrophy (choice D) is a disorder of myelin metabolism. It is characterized by the accumulation of galactosyl sulfatide (cerebroside sulfate). Symptoms may appear at any age and include mental regression, urinary incontinence, blindness, loss of speech, peripheral neuropathy, and seizures. Sandhoff- Jatzkewitz disease (choice E) is a disorder related to Tay-Sachs disease. It is characterized by a defect in the degradation of GM2 gangliosides with symptoms of severe mental retardation, blindness, and early mortality.

QUESTION 197
Interference with the action of angiotensinconverting enzyme (ACE) is an effective means at reducing elevations in blood pressure. The circulating concentration of which of the following hormones would be affected as a consequence of the use of ACE inhibitors?

A. ACTH
B. aldosterone
C. corticotrophin-releasing hormone, CRH
D. estradiol
E. gonadotropin-releasing hormone, GnRH

Correct Answer: B
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
ACE is responsible for the cleavage of two amino acids from angiotensin I, generating angiotensin II. Angiotensin II is a peptide hormone of the rennin-angiotensin system responsiblefor regulation of blood pressure. The intra-renal baroreceptor system is a key mechanism for regulating renin secretion. Adrop in pressure results in the release of renin from the juxtaglomerular cells of the kidneys. Renin secretion is also regulated by the rate of and transport across the macula densa.

The higher

Na^+

the rate of transport of these ions, the lower is the rate of renin secretion. The only function for renin is to cleave a 10-amino acid peptide from the N-terminal end of angiotensinogen-yielding angiotensin I. ACE action then generates angiotensin II, one of the most potent naturally occurring vasoconstrictors. In addition to the vascular effects, other physiological responses to angiotensin II include induction of adrenal cortex synthesis and secretion of aldosterone. Release of aldosterone leads to further Na+ retention by the kidneys with the consequences being an additional pressive effect on the vasculature. Thus, the use of ACE inhibitors would not only reduce the production of angiotensin II but also aldosterone. Synthesis and secretion of none of the other hormones (choices A, CE) would be affected by ACE inhibitor administration.

QUESTION 198
AIP is the major autosomal-dominant acute hepatic porphyria. This disease is caused by a deficiency in porphobilinogen (PBG) deaminase, an enzyme of heme biosynthesis. Patients afflicted with this disease would be expected to excrete excess amounts of which of the following?

A. delta-aminolevulinic acid (ALA)
B. coproporphyrinogen III
C. hydroxymethylbilane
D. protoporphyrin IX
E. type III uroporphyrinogen

Correct Answer: A
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
PBG deaminase (also called hydroxymethylbilane synthase) catalyzes the heme biosynthesis reaction involving the head-to-tail condensation of four molecules of PBG to produce the linear tetrapyrrole intermediate, hydroxymethylbilane. Hydroxymethylbilane can nonenzymatically cyclize into uroporphyrinogen I, which is why PBG deaminase is also known as uroporphyrinogen I synthase. ALA is the precursor for PBG, thus a defect in PBG deaminase would lead to excess ALA excretion. The compounds in choices BE all represent products of reactions that are downstream of PBG deaminase in the heme biosynthetic pathway and thus would not be excreted in high amounts in someone with AIP.

QUESTION 199
In a comparative study of two related cell lines, you find that one responds normally to insulin while the other has an impaired response. You discover that both cell lines bind insulin with equal affinity but that the impaired response is manifest in an inability to recruit the insulin response substrate-1 (IRS-1) protein to the receptor. This would most likely be due to which of the following?

A. inability of the receptor to phosphorylate the RAS G-protein
B. loss of activation of phospholipase C-gamma (PLC-g)

C. mutation in the tyrosine phosphorylation site of IRS
D. serine phosphorylation of the insulin receptor preventing IRS binding
E. tyrosine phosphorylation of the insulin receptor leading to the loss of the IRS binding site

Correct Answer: C
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Many causes of insulin-resistance are due to defects that occur in events of the insulininduced signaling cascade, which takes place after insulin binds to its receptor. All of the postreceptor responses initiated by insulin binding to its receptor are mediated as a consequence of the activation of several signal transduction pathways that require tyrosine phosphorylation of sites in the intracellular portion of the receptor. These include receptor activation of PI3K. Activation of PI3K involves a linkage to receptor activation of insulin receptor substrates (of which there are four: IRS-1, IRS-2, IRS-3, and IRS-4). Activated PI3K phosphorylates membrane phospholipids, the major product being phosphotidylinositol 3,4,5-trisphosphate, PIP3. PIP3 in turn activates the enzymes protein kinase B, PKB (also called Akt), PIP3-dependent kinase (PDK), some isoforms of PKC, principally PKC-l, and small ribosomal subunit protein 6 kinase, S6K. The mitogen-activated protein (MAP) kinase pathway is also activated either through receptor activation of the protein tyrosine phosphatase (Shp-2) or growth factor receptor- binding protein-2 (Grb2). With respect to insulin responses, activation of PKB and PKC-l leads to translocation of GLUT4 molecules to the cell surface. resulting in increased glucose uptake which is significant in skeletal muscle. Activation of PKB also leads to the phosphorylation and activation of GSK3, which is a major regulatory kinase of glycogen homeostasis. In addition, PKB phosphorylates and inhibits the activity of a transcription factor (FKHRL1) that has proapoptotic activity. This results in reduced apoptosis in response to insulin action. Activation of S6K leads to the phosphorylation of the regulator of translation eIF-4E-binding protein, 4E-BP. Phosphorylation of 4E-BP prevents it from binding to eIF-4E, the consequences of which would normally lead to a reduction in translation rate. Insulin also has profound effects on the transcription of numerous genes, effects that are primarily mediated by regulated function of sterol-regulated element-binding protein (SREBP). These transcriptional effects include (but are not limited to) increases in glucokinase, PK, LPL, FAS, and ACC and decreases in glucose-6-phosphatase, fructose-1,6-bisphosphatase, and PEPCK. The insulin receptor does not phosphorylate the RAS gene product (choice A). Loss of activation of PLC-g (choice B) would not prevent IRS proteins from binding to the activated insulin receptor. Serine phosphorylation of the insulin receptor (choice D) is not involved in IRS binding. Tyrosine phosphorylation of the insulin receptor results in the formation of IRS binding sites, not in the loss (choice E) of such binding sites.

QUESTION 200
There is but a single enzyme-catalyzed reaction in the human body known to generate carbon monoxide (CO) as one of its products. Which of the following enzymes represents the one that catalyzes this CO-producing reaction?

A. biliverdin reductase
B. coproporphyrinogen oxidase
C. heme oxygenase
D. protoporphyrinogen oxidase
E. uroporphyrinogen decarboxylase

Correct Answer: C
Section: Biochemistry

Explanation

Explanation/Reference:
Explanation:
Heme is oxidized, with the heme ring being opened by the endoplasmic reticulum enzyme, heme oxygenase (see below figure). The oxidation step requires heme as a substrate, and any hemin

(Fe^{3+})

is reduced to heme prior to oxidation by heme oxygenase. The oxidation occurs on a specific

(Fe^{2+})

carbon producing the linear tetrapyrrole biliverdin, ferric iron , and CO. This is the only

(Fe^{3+})

reaction in the body that is known to produce CO. Most of the CO is excreted through the lungs, with the result that the CO content of expired air is a direct measure of the activity of heme oxidase in an individual. Biliverdin reductase (choice A) catalyzes the conversion of biliverdin to bilirubin as shown in figure. Coproporphyrinogen oxidase (choice B), protoporphyrinogen oxidase (choice D), and uroporphyrinogen decarboxylase (choice E) are all involved in the synthesis of heme and do not produce CO in the course of catalyzing their reactions.

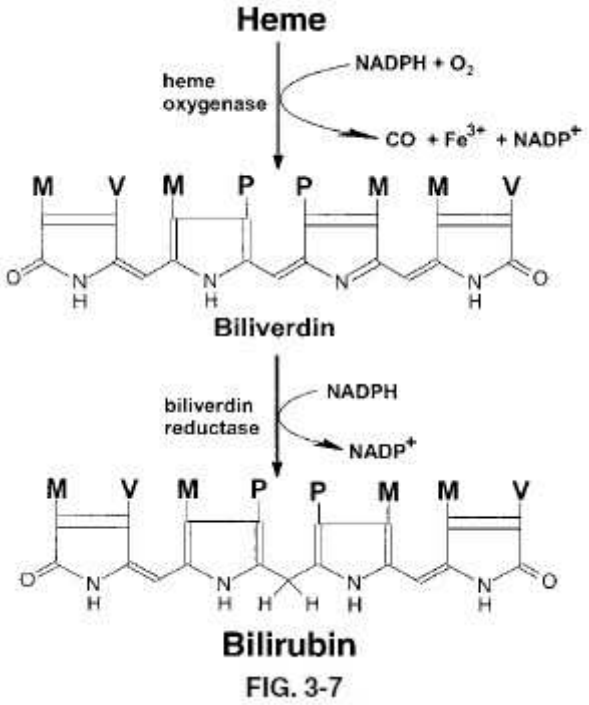


FIG. 3-7

QUESTION 201
An infant admitted to the emergency room has been found to be suffering from ammonia intoxication, which was verified by measurement of an elevation of N + in the serum. Treatment of this infant

H_4

with arginine results in a reduction serum N + and a lessening of the effects of the ammonia

H_4

toxicity. The ability of arginine to render this effect stems from its role in the synthesis of an allosteric activator of the the urea cycle enzyme, carbamoylphosphate synthetase-I (CPS-I). Which of the following represents this potent allosteric effector of CPS-I?

A. argininosuccinate
B. bicarbonate ion

C. fumarate
D. N-acetylcysteine
E. N-acetylglutamate

Correct Answer: E
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
CPS-I is absolutely dependent on the allosteric effector N-acetylglutamate for its activity. This allosteric effector is synthsized by the enzymeN-acetylglutamate synthetase, which is activated by the urea cycle amino acid arginine. None of the other compunds (choices A, B, C, and D) have any effect on CPS-I activity.

QUESTION 202
Which of the following peptide hormones is released in response to stimulation of pituitary gonadotropes?

A. ACTH
B. follicle-stimulating hormone
C. growth hormone
D. prolactin
E. thyroid-stimulating hormone

Correct Answer: B
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
The pituitary gonadotrophs are cells that secrete the gonadotrophic peptide hormones, follicle- stimulating hormone (FSH), and leutinizing hormone (LH). FSH acts on Sertoli cells of the testis inducing androgen-binding protein synthesis, which maintains a high concentration of testosterone in tubules increasing spermatogenesis. In the ovary, FSH stimulates aromatase activity in the granulose cells stimulating ovum maturation and estradiol production. Pituitary orticotrophs are the ACTH- secreting cells (choice A), somatotrophs secrete growth hormone (choice C), lactotrophs secrete prolactin (choice D), and thyrotrophs secrete thyroid-stimulating hormone (choice E).

QUESTION 203
The rate-limiting step in glycolysis occurs at the step catalyzed by which of the following enzymes?

A. glyceraldehyde-3-phosphate dehydrogenase
B. 6-phosphofructo-1 kinase, PFK-1

C. 6-PFK-2
D. phosphoglycerate kinase
E. pyruvate kinase

Correct Answer: B
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
There are three reactions of glycolysis that are thermodynamically irreversible. These are the hexokinase (glucokinase), PFK-1, and PKcatalyzed reactions. Reactions that are essentially irreversible in most metabolic pathways are subject to complex regulatory controls and represent rate-limiting steps in the pathway. The primary site of regulation of glycolysis occurs at the level of the PFK-1-catalyzed step. Hence, this reaction is the rate-limiting step in glycolysis. PFK-1 is subject to allosteric control by numerous compounds. Citrate and ATP inhibit the activity of PFK-1, while AMP and fructose 2,6- bisphosphate (F2,6-BP) activate the enzyme. The principal control of PFK-1 activity is exerted by alterations in the level of F2,6-BP. This compound is synthesized from fructose-6-phosphate by the bifunctional enzyme, PFK-2/fructose-2,6-bisphosphatase (PFK-2/F2,6-BPase). PFK-2 (choice C) contains two catalytic domains, one a kinase and the other a phosphatase, the activities of which are affected by the state of phosphorylation. The phosphatase domain is active when the enzyme is phosphorylated and converts F2,6-BP back to F6-P, thereby reducing the levels of this powerful activator of PFK-1. Thus, although the activity of PFK-2 will determine the rate of activity of PFK-1, it is itself not the rate-limiting enzyme in glycolysis. Glyceraldehyde-3-phosphate dehydrogenase (choice A) and PGK (choice D) are not regulated enzymes of glycolysis. PK (choice E) is regulated during glycolysis, but does not constitute a rate-limiting step.

QUESTION 204
The statin class of drugs that are currently used to control hypercholesterolemia function to lower circulating levels of cholesterol by which of the following mechanisms?

A. increasing the elimination of bile acids, leading to increased diversion of cholesterol into bile acid production
B. increasing the synthesis of apolipoprotein B-100 (apo), resulting in increased elimination of cholesterol through the action of low-density lipoprotein (LDL) uptake by the liver
C. decreasing the absorption of dietary cholesterol from the intestines
D. inhibiting the interaction of LDLs with the hepatic LDL receptor
E. inhibiting the rate-limiting step in cholesterol biosynthesis

Correct Answer: E
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
The statin class of cholesterol-lowering drugs all exert their effects on the activity of HMG-CoA reductase. This enzyme carries out the rate-limiting step in cholesterol biosynthesis. The cholestyramine-based resins are used therapeutically to bind up intestinal bile salts, which increases the excretion of bile (choice A).

The net effect of increased bile excretion is increased diversion of cholesterol into bile acid synthesis, thereby lowering circulating cholesterol levels. No current therapy targets synthesis of apolipoprotein synthesis (choice B), decreasing intestinal absorption of cholesterol (choice C), or inhibition of LDL-receptor interactions (choice D).

QUESTION 205
Which of the following represents the enzyme deficiency that leads to "essential fructosuria"?

A. fructose-1-phosphate aldolase (aldolase B)
B. fructose-1,6-bisphosphate aldolase (aldolase A)
C. fructokinase
D. hexokinase
E. 6-PFK-1

Correct Answer: C
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Essential fructosuria is an autosomal recessive disorder manifesting benign asymptomology due to a lack of fructokinase. The principal clinical signs of essential fructosuria are hyper-fructosemia and fructosuria. Deficiency in aldolase B (choice A) results in the clinically severe disorder, hereditary fructose intolerance. Symptoms include severe hypoglycemia and vomiting after ingestion of fructose. Prolonged fructose ingestion by infants with this disorder will lead to poor feeding, hepatomegaly, vomiting, jaundice, and eventually hepatic failure and death. Aldolase A deficiency (choice B) is very rare and has only been observed associated with erythrocytes and fibroblasts and leads to hemolytic anemia. Hexokinase deficiency (choice D) is also rare and associated with erythrocyte disfuction leading to chronic hemolytic anemia. Deficiency in PFK-1 (choice E) results in the glycogen storage disease known as Tarui disease. Symptoms of PFK-1 deficiency include exercise-induced cramping and pain, myoglobinuria, and hemolytic anemia.

QUESTION 206
Clinical evidence indicates aspirin is effective in the control of numerous chronic conditions such as atherosclerosis. The principal cardiovascular benefit from aspirin is due to its ability to reduce the incidence and severity of thrombotic episodes. The anticoagulant effect of aspirin occurs through its ability to inhibit which of the following activities?

A. cyclooxygenase
B. fibrin cross-linking by factor XIIIa
C. phospholipase
D. thrombin binding to activated platelets
E. von Willebrand factor

Correct Answer: A

Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
The synthesis of the cyclic eicosanoids (the prostaglandins and the thromboxanes) begins with the cyclization of arachadonic acid. This reaction is carried out by the enzyme prostaglandin endoperoxide synthetase. This enzyme has two distinct activities, cyclooxygenase and a peroxidase. The activity of the cyclooxygenase domain is inhibited by a class of compounds referred to as the NSAIDs. Aspirin is of this class of drug and, therefore, inhibits the cyclooxygenase activity. The inhibition of prostaglandin synthesis has a negative effect on the process of coagulation through a reduction in the production of , a potent activator of platelet function. Aspirin also reduces the production of prostacyclin

TXA_2

by endothelial cells. is a vasodilator and an inhibitor of platelet aggregation. Since

PGI_2

endothelial cells regenerate active cyclooxygenase faster than platelets, the net effect of aspirin is more in favor of endothelial cellmediated inhibition of the coagulation cascade. The action of the steroidal anti-inflammatory drugs occurs through the inhibition of phospholipase (choice C), and inhibition

A_2

of this enzyme has no direct effect on the coagulation process. The other choices (B, D, and E) are not targets for the action of aspirin.

QUESTION 207
Gluconeogenesis is an extremely important reaction carried out in hepatocytes allowing for glucose homeostasis in the blood. The primary positive control of hepatic gluconeogenesis is exerted by which of the following?

A. high acetylcoenzyme A (acetyl-CoA) levels
B. high adenosine triphosphate (ATP) levels
C. high citrate levels
D. low ATP levels
E. low citrate levels

Correct Answer: A
Section: Biochemistry
Explanation

Explanation/Reference:

Explanation:
The first step in gluconeogenesis is the formation of oxaloacetate from pyruvate. The enzyme controlling this step is pyruvate carboxylase, an allosteric enzyme that does not function in the absence of its primary effector, acetyl-CoA, or closely related acyl-CoA. Thus, a high level of acetyl-CoA signals the need for more oxaloacetate. If there is a surplus of ATP, oxaloacetate will be used for gluconeogenesis. Under conditions of low ATP, oxaloacetate will be consumed in the citric acid cycle. Citrate is the primary negative effector of glycolysis and the primary positive effector of fatty acid synthesis. High levels of citrate (choice C), but not low levels (choice E), do positively affect the activity of fructose-1,6-bisphosphatase, one of the bypass enzymes of gluconeogenesis, but this is not the primary site of control, since the carbon atoms must first go through the pyruvate carboxylase reaction. Low ATP levels (choice D) would be reflected in an elevation in ADP levels, and ADP negatively affects the activity of pyruvate carboxylase. High ATP levels (choice B) are necessary in order for gluconeogenesis to proceed, and will negatively affect glycolysis at the level of PFK-1, allowing for an increased net flow of carbon into glucose. However, increased levels of ATP do not directly regulate the enzymes of gluconeogenesis.

QUESTION 208
A6-month-old who is failing to thrive is brought to your clinic. Tests reveal hepatosplenomegaly, muscle weakness and atrophy, hypotonia, and decreased deep tendon reflexes. Blood tests reveal that the infant has normal glucose levels. Biopsy of the liver reveals initial stages of cirrhosis due to the accumulation of an abnormal glycogen with few branch points, whose structure resembles amylopectin. The clinical and laboratory results presented are indicative of which glycogen storage disease?

A. Andersen disease (type IV glycogen storage disease)
B. Cori or Forbes disease (type III glycogen storage disease)
C. McArdle disease (type V glycogen storage disease)
D. Tarui disease (type VII glycogen storage disease)
E. von Gierke disease (type I glycogen storage disease)

Correct Answer: A
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Andersen disease (also referred to as type IV glycogen storage disease) manifests its symptoms as a result of the accumulation of glycogen, with unbranched long outer chains in tissues. This structure of glycogen resembles that of plant amylopectin. Symptoms appear within the first year of life and lead to failure to thrive and pronounced heptosplenomegaly. Hypoglyemia is rarely seen with this disorder. Cori disease (choice B) affects both liver and muscle with accumulations of glycogen that has short outer chains (resembles limit dextrin). Symptoms include hepatomegaly, hypoglycemia, hyperlipidemia, and retarded growth. McArdle disease (choice C) usually manifests in adulthood and characteristic symptoms include exercise intolerance, muscle cramping with exercise, and myoglobinuria. The affected tissue in this disease is only skeletal muscle. Tarui disease (choice D) also affects skeletal muscle and as such manifests with clinical symptoms very similar to those of McArdle disease with the exceptions that Tarui patients also experience hemolytic anemia and myogenic hyperuricemia. Symptoms of von Gierke disease (choice E) result from the excessive accumulation of glycogen in liver, kidney, and intestinal mucosa. Symptoms include growth retardation, hypoglycemia, heptomegaly, hyperlipidemia, lactic acidemia, and hyperuricemia.

QUESTION 209
Analysis of a tumor cell line indicates that there is a dramatically increased level in the activity of the transcription factor E2F. Which of the following is the most

likely explanation for this observation?

A. an increase in the expression of pRB resulting in increased binding of pRB to E2F
B. hypophosphorylation of pRB so that it can no longer interact with E2F
C. loss of expression of pRB which normally activates E2F
D. mutation in pRB that prevents its phosphorylation so that it cannot interact with the gene to which it normally binds and coactivates with E2F
E. mutation in the domain of pRB to which E2F binds, the consequences of which lead to constitutive E2F activity

Correct Answer: E
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Members of the E2F family of transcription factors play critical roles in regulating cell-cycle transit through the G1-S restriction point. The activity of E2F is regulated by interaction with the protein product of the retinoblastoma susceptibility tumor suppressor gene, pRB. Interaction of pRB and E2F occurs when pRB is in a hypophosphorylated state (below figure).

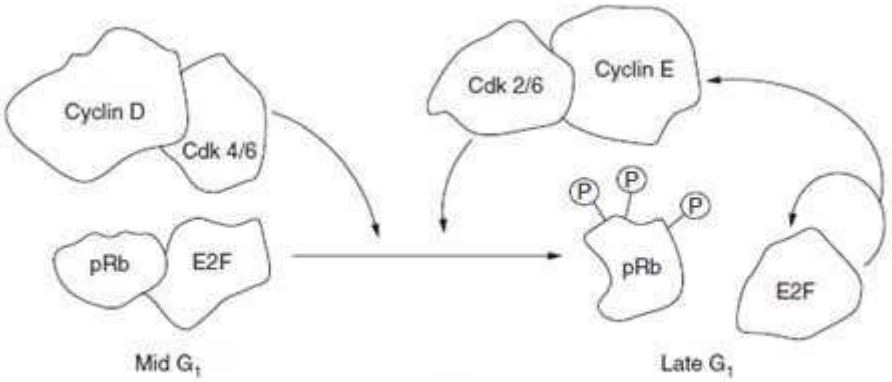


FIG. 3-8

Members of the cyclin-dependent kinase family of cell-cycle regulating kinases target pRB for phosphorylation. When phosphorylated, pRB dissociates from E2F allowing E2F to enter the nucleus and transcriptionally activate genes involved in DNA synthesis, as well as activate its own transcription. Transcription of both cyclin E and CDK2 are activated by E2F. These two proteins form a complex that promotes progression through S-phase of the cell cycle and also act to keep E2F active by adding to the phosphorylation state of pRB (below figure). Thus, any defect in the ability of pRB to bind to E2F will lead to constitutive activation of DNA synthesis leading to unrestrained proliferation. None of the other options (choices AD) represent viable phenomena to account for the observed increase in E2F activity.

QUESTION 210
Chromatin remodeling is associated with alterations in the transcriptional activity of genes in the region of the remodeling. Which of the following statements is most correct concerning the events of chromatin remodeling?

A. Chromatin remodeling occurs predominantly in regions enriched in CpG dinucleotides.
B. Histone acetylation tends to destabilize chromatin structure.
C. Methylation of cytosine residues induces the remodeling event.
D. Methylation of histone H1 is sufficient to stimulate remodeling.
E. Remodeling is necessary to induce the property of genomic imprinting.

Correct Answer: B
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
The posttranslational modification of histone proteins has considerable effect on numerous activities at the level of the chromatin. In particular, the acetylation and/or methylation of histones in the nucleosome (H2A, H2B, H3, and H4) results in an altered stability of the 30-nm chromatin fiber as well as other higher order chromatin structure. No specific regions of remodeling have been identified relative to sequence content such as CpG islands (choice A). Methylation of cytosine residues in the DNA (choice C) has an effect on transcriptional activity but not on chromatin structure. Methylation of the linker histone, H1 (choice D) has not been demonstrated. Chromtin remodeling does not direct imprinting (choice E). Imprinting is regulated by the state of DNA methylation.

QUESTION 211
A 4-month-old Caucasian male infant with a temperature of 38.4℃ is examined by his pediatrician. His mother indicates that he has had the fever for the past 4 days, been listless, vomiting, and has watery stools. Blood work indicates the infant is hypoglycemic but this condition does not respond to either epinephrine or glucose administration. In addition, his blood pH is slightly acidic and shows reduced bicarbonate. Other untoward blood chemistry includes elevated triglycerides, cholesterol, and liver enzymes. The child has a protruberant abdomen, thin extremities, and a doll-like face. The pediatrician suspects a specific condition and orders a liver biopsy to test for the activity of which of the following enzyme activities?

A. glucose-6-phosphatase
B. glycogen synthase
C. muscle phosphofructokinase
D. muscle phosphorylase
E. pyruvate kinase

Correct Answer: A
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Deficiency in glucose-6-phosphatase (choice A) is one cause of glycogen storage disease type I (specifically type Ia, von Gierke disease). Hallmarks of the disease are hypoglycemia, lactic acidosis, hyperuricemia, and hyperlipidemia. If symptoms do not appear until the third or fourth month they include hepatomegaly and hypoglycemic seizures. Afflicted children have a protruberant abdomen due to the massive hepatomegaly. Outward physical signs also include extremely thin extremities, short stature, and chubby doll-like faces. Liver glycogen synthase deficiency (choice B) presents with morning fatigue and ketotic hypoglycemia on fasting--both of which rapidly disappear on feeding. Symptoms can be rapidly relieved and chemical signs corrected by introducing frequent protein-rich meals and nighttime feedings of suspensions of uncooked corn starch. Adeficiency in muscle phosphofructokinase (choice C) results in glycogen storage disease type VII (Tarui disease). Clinically, the symptoms seen in Tarui disease are very similar to those seen in muscle phosphorylase deficiency (choice D), glycogen storage disease type V (McArdle disease) such as exercise-induced cramping and early fatigue. There are five clinical characteristics allowing distinction betweeen Tarui and McArdle disease: exercise intolerance is evident in childhood and more severe and is associated with nausea and vomiting; the intolerance is particularly acute following meals rich in carbohydrates; hyperuricemia is more severe; compensated hemolytic anemia is evidenced by increased serum bilirubin and reticulocyte count, and lastly; an abnormal polysaccharide is present in muscle fibers. Deficiency in PK (choice E) is the most common enzyme deficiency leading to hemolytic anemia and the disorder is characterized by lifelong episodes. The most severe deficiency will result in embryonic lethality.

QUESTION 212
When cells acquire sufficient energy such that the rate of flux through the tricarboxylic acid (TCA) cycle declines, excess acetyl-CoA that cannot be oxidized is predominantly converted into fat. In order for the carbons in mitochondrial acetyl-CoA to serve as a precursor for fat synthesis, they must be delivered to the cytosol. Which of the following represents the molecule used to transport acetyl-CoA to the cytosol?

A. acetyl-CoA
B. carnitine
C. citrate
D. beta-hydroxybutyrate
E. pyruvate

Correct Answer: C
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Acetyl-CoA cannot freely diffuse across the membranes of the mitochondria, nor is there a transport mechanism to move the molecule to the cytosol. This ensures that all acetyl-CoA generated by PDH or fat oxidation will be used for energy production. However, as cellular energy demand falls, carbon atoms can be diverted into storage molecules such as glycogen and fatty acids. To move acetyl-CoA out of the mitochondria to the cytosol it must first be converted to citrate, which can be ransported by the TCA transport system (below figure).

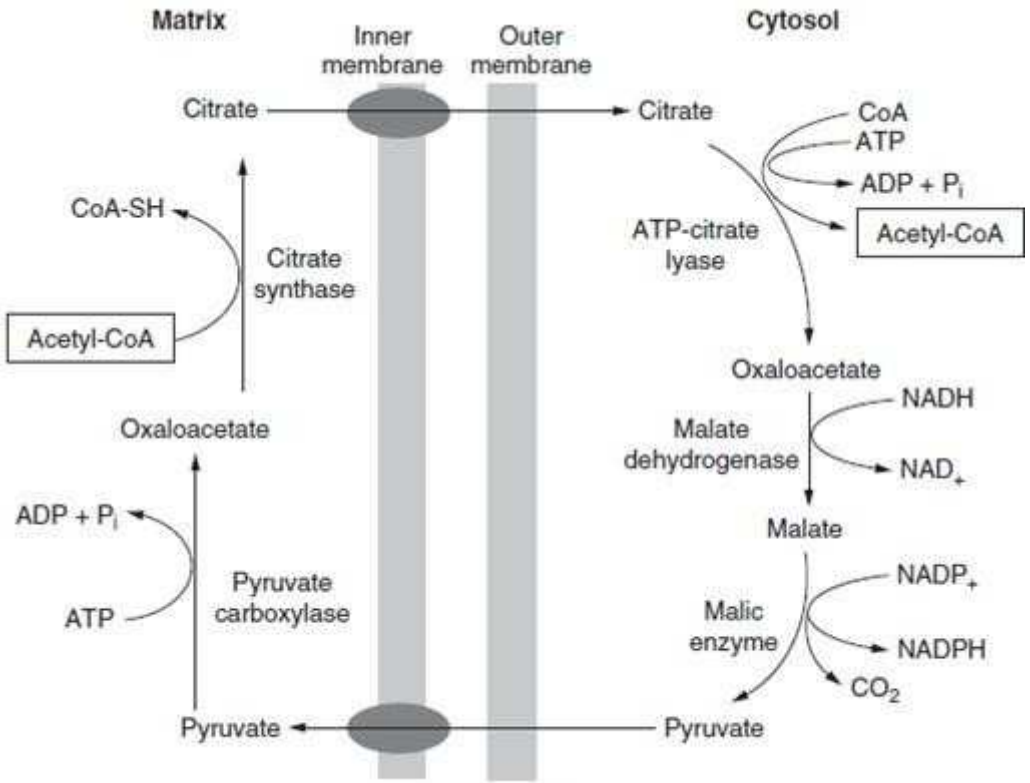


FIG. 3-9

As indicated, acetyl-CoA (choice A) is "trapped" inside the mitochondria. Carnitine (choice B) is necessary for transport of fatty acids into the mitochondria prior to their oxidation, but plays no role in acetyl-CoA transport. Ketone bodies such as beta-hydroxybutyrate (choice D) are generated in hepatic mitochodria when acetyl-CoA is in excess. However, usage of ketone bodies by nonhepatic tissues involves conversion to acetyl-CoA with the mitochondria, not the cytosol. Pyruvate (choice E) can be transported into the mitochondria but not out.

QUESTION 213
Which of the following is true with respect to the actions of the mineralocorticoids?

A. decrease carbohydrate metabolism
B. increase appearance of the secondary sex characteristics
C. increase synthesis of androgens
D. regulate aldosterone secretion

E. regulate sodium retention by the kidneys

Correct Answer: E
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
The principal mineralocorticod, produced by the zona glomerulosa cells of the adrenals, is aldosterone. Synthesis of aldosterone is primarily controlled by the rennin-angiotensin system and is thus involved in control of blood pressure. Aldosterone causes sodium reabsorption by the kidneys, which in turn regulate water balance, which leads to increases in blood pressure by increasing fluid volume. Aldosterone action does not directly lead to decreased carbohydrate metabolism (choice A), is not a sex characteristic determining steroid hormone (choice B), does not result in increased synthesis of androgens (choice C), and does not regulate its own secretion (choice D).

QUESTION 214
A 9-month-old child is presented to the emergency room by his parents who report that he has been vomiting and has severe diarrhea. The episodes of vomiting began when the parents started feeding their child cow's milk. The infant exhibits signs of failing to thrive. Laboratory tests show elevated blood galactose, hypergalactosuria, metabolic acidosis, albuminuria, and hyperaminoaciduria. These clinical and laboratory findings are most consistent with which of the following disorders?

A. alkaptonuria
B. essential fructosuria
C. hereditary galactosemia
D. Menkes disease
E. von Gierke disease

Correct Answer: C
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Severe hereditary galactosemia presents in the first few months of life with symptoms that include poor feeding and associated weight loss, vomiting, diarrhea, lethargy, and hypotonia. Clinical findings will include those presented in the case. The symptoms are aggravated by consumption of cow's milk and can be resolved provided proper diagnosis is made and treatment is started early. Alkaptonuria (choice A) results from the accumulation of homogentisic acid, a by-product of tyrosine catabolism, in the urine and tissues. Oxidation of homogentisate in the urine causes it to turn dark and in the tissues results in ochronosis, which refers to the ochre color of the deposits in connective tissue, bones, and other organs. Essential fructosuria (choice B) is a benign asymptomatic metabolic disorder manifesting with alimentary hyper-fructosemia and fructosuria. Menkes disease (choice D) results from a defect in intracellular copper transport and the symptoms of the disease are caused by loss of function of copper- dependent enzymes. Symptoms include abnormal (kinky) hair and pigmentation, cerebral degeneration, failure to thrive, and skin laxity. Symptoms of von Gierke disease (choice E) result from the excessive accumulation of glycogen in liver, kidney, and intestinal

mucosa. Symptoms include growth retardation, hypoglycemia, heptomegaly, hyperlipidemia, lactic acidemia, and hyperuricemia.

QUESTION 215
Continued consumption of calories in excess of energy expenditure will eventually lead to obesity, a current major health problem in the United States. A major contributing factor in obesity is a disorder in fuel partitioning, as evidenced by a lower rate of fat oxidation in obese individuals. Which of the following situations would best explain a reduction in overall fat metabolism in these individuals?

A. An increase in the hepatic ATP/ adenosine diphosphate (ADP) ratio increases incorporation of carbon into fatty acids by causing an inhibition in acetyl-CoA oxidation in the TCA cycle.
B. Decreased hepatic gluconeogenesis which requires acetyl-CoA from fatty acid oxidation, thus fat oxidation is secondarily inhibited.
C. Increased levels of malonyl-CoA occur in these individuals leading to inhibition of carnitine palmitoyltransferase I.
D. Insulin-induced decrease in the activity of acetyl-CoA carboxylase (ACC) causing reduction in fatty acid synthesis.
E. Insulin-induced repression of fatty acid synthase (FAS) activity.

Correct Answer: C
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
The oxidation of long-chain fatty acids is initiated by the sequential action of carnitine palmitoyltransferase-I (CPTI), which is located in the outer mitochondrial membrane, and carnitine palmitoyltransferase II, which is located in the inner mitochondrial, together with a carnitine- acylcarnitine translocase. Major control over the process is exerted at the level of CPTI by virtue of the unique inhibitability of this enzyme by malonyl-CoA. Thus, CPTI has a pivotal role in lipid metabolism. Obese individuals have higher overall dietary intake of lipid and the disruption in fat metabolism exacerbates the increases in malonyl-CoA, which propagates the fuel partitioning disorder. Although an increase in hepatic ATP (choice A) will lower the flux through the TCA cycle, this does not constitute a mechanism for a disruption in fuel partitioning. The rate of hepaticgluconeogenesis (choice B) does not significantly affect fat metabolism. Obese individualsactually have reduced responses to insulin (choiceD) and thus any insulin-mediated effects on ACC would be minimal.
Insulin does not repress FAS activity (choice E).

QUESTION 216
A3-month-old infant who otherwise appeared normal during the first 2 months of life except for a bout of hyperbilirubinemia is now clearly exhibiting developmental delay. In addition, the infant's hair has become grayish and dull and there is a stubble of broken hair over the occiput and temporal regions. The facial appearance has also changed such that the infant has very pudgy cheeks, abnormal eyebrows, and sagging jowls. The occurrence of frequent convulsions was the stimulus for the parents to bring their child to the emergency room. These rapidly deteriorating symptoms are indicative of which of the following disorders?

A. Crigler-Najjar syndrome type I
B. Gilbert syndrome
C. hemochromatosis
D. Menkes disease

E. Refsum disease

Correct Answer: D
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Menkes disease is an X-linked recessive disorder that is manifest by a defect in copper absorption. This defect leads to dysfunction of numerous enzymes that need copper as a cofactor, leading to the typical symptoms observed in this patient. In fact, Menkes disease is also referred to as steely hair disease, because of the characteristic brittleness of the hair, which is easily broken. Crigler-Najjar syndrome type I (choice A) is also due to defective bilirubin metabolism as a result of a loss of UDP- glucuronosyltransferase (UGT) activity. UGT is required to transfer 2 moles of glucuronic acid to bilirubin, generating bilirubindiglucuronide, which makes bilirubin much more water soluble and therefore facilitates its excretion. Crigler-Najjar syndrome results in nonhemolytic icterus (jaundice) within the first few days of life and is generally fatal during neonatal life due to severe kernicterus. Gilbert syndrome (choice B) results from a defect in bilirubin metabolism. It is typically diagnosed in young adults and is characterized by mild, chronic, and unconjugated hyperbilirubinemia without associated hemolysis. Hemochromatosis (choice C) is the term applied when organ structure and function are impaired by the presence of excess amounts of iron. The liver, heart, pancreas, skin, joints, and endocrine organs are the principal tissues affected by iron accumulation. Symptoms include cirrhosis, cardiomyopathy, arthritis, abnormal skin pigmentation, and hypogonadism, as well as diabetes mellitus. Refsum disease (choice E) results from a defect in the metabolism of phytanic acid, a plant lipid which must be oxidized by a separate pathway from that of animal fats. Cardinal symptoms include retinitis pigmentosa, peripheral neuropathy, and cerebellar ataxia.

QUESTION 217
Presentation of the platelet membrane protein complex, GPIIb-GPIIIa, which binds with von Willebrand factor, is necessary for which of the following?

A. activation of PKC leading to phosphorylation of myosin light chain and platelet morphology changes
B. cleavage and activation of high molecular weight kininogen
C. inducing platelet crosslinking
D. release of thrombin from platelet granules
E. stimulation of endothelial and smooth muscle cell interaction resulting in vasoconstriction

Correct Answer: C
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
The platelet membrane glycoprotein complex, GPIIb-GPIIIa, is a receptor for fibrinogen. Presentation of GPIIb-GPIIIa on the surface of activated platelets leads to platelet crosslinking. The cross-linking occurs between activated platelets that are adhered to the endothelial cell surface via interaction of the platelet surface complex GPIa-GPIIa with exposed collagen, as well as between platelets in the local circulation. The effect is to ensure that a loose platelet plug forms rapidly at the site of vascular injury stemming the flow of blood until a fibrin clot can be formed. Activation of platelet PKC (choice A) is the consequence of thrombin binding to platelet thrombin receptors. Cleavage of high molecular weight kininogen (choice B) occurs upon the activation of factor XII. Release of thrombin from platelet

alpha granules (choice D) occurs in response to platelet activation. Activation of platelets must first occur in order for GPIIb- GPIIa to be presented on the surface and, thus, this glycoprotein complex is not directly involved in platelet activation and granule release. Vasoconstriction, in concert with hemostasis (choice E), occurs primarily as a result of the action of serotonin released from alpha granules of activated platelets.

QUESTION 218
Synthesis of glycogen is inhibited in hepatocytes in response to glucagon stimulation primarily as a result of which of the following?

A. a decrease in the level of phosphoprotein phosphatase
B. a decrease in the level of phosphorylated phosphorylase kinase
C. a decrease in the levels of phosphorylated phosphoprotein phosphatase inhibitor-1
D. an increase in the level of the dephosphorylated form of glycogen synthase
E. an increase in the level of the phosphorylated form of glycogen synthase

Correct Answer: E
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Glucagon is released from the pancreas in response to low blood glucose and stimulates hepatocytes to synthesize glucose for delivery to the blood. Therefore, it would be counterproductive for hepatocytes to divert any of the gluconeogenically derived glucose into glycogen. This is accomplished by inhibition of glycogen synthase. Glucagon exerts its effects on the liver through the glucagon receptor. When glucagon binds, the receptor activates adenylate cyclase leading to increased production of cAMP. In turn, cAMP activates cAMP-dependent protein kinase, which then phosphorylates a number of substrates. Glucagon has no effect on the level of phosphoprotein phosphatase (choice A). One of the substrates of PKA is glycogen synthase/phosphorylase kinase. Therefore, there would not be a decrease in the level of phosphorylated phosphorylase kinase (choice B). In turn, synthase/phosphorylase kinase phosphorylates glycogen phosphorylase and glycogen synthase. Therefore, there is no increase in the level of dephosphorylated glycogen synthase (choice D). Phosphorylation inhibits glycogen synthase activity and activates phosphorylase. In addition, PKA itself can phosphorylate glycogen synthase. The net effect is an increase in the rate of glucose phosphorolysis from glycogen and a reduced incorporation of glucose into glycogen. An additional PKA substrate is phosphoprotein phosphatase inhibitor-1, and therefore therewould not be a decrease in the level of the phosphorylated form of this enzyme (choice C).

QUESTION 219
Which of the following occurs in the lipidosis known as Tay-Sachs disease?

A. Ganglioside GM2 is not catabolized by lysosomal enzymes.
B. Phosphoglycerides accumulate in the brain.
C. Synthesis of a specific ganglioside is decreased.
D. Synthesis of a specific ganglioside is excessive.
E. Xanthomas, due to cholesterol deposition, are observed.

Correct Answer: A
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
In the genetic disorder known as Tay-Sachs disease, ganglioside is not catabolized. As a

GM_2

consequence, the ganglioside concentration is elevated many times higher than normal. The functionally absent lysosomal enzyme is beta- N-acetylhexosaminidase. The elevated results in

GM_2

irreversible brain damage to infants, who usually die before the age of 3 years. Under normal conditions, this enzyme cleaves N-acetylgalactosamine from the oligosaccharide chain of this complex sphingolipid, allowing further catabolism to occur. The cause of most lipidoses (lipid storage diseases) is similar. That is, a defect in catabolism of gangliosides causes abnormal accumulation. None of the other choices (B, C, D, and E) result in glycosphinogolipidoses such as is characteristic of Tay-Sachs disease.

QUESTION 220
In Type I diabetes, the increased production of ketone bodies is primarily a result of which of the following?

A. a substantially increased rate of fatty acid oxidation by hepatocytes
B. an increase in the rate of the citric acid cycle
C. decreased cyclic adenosine monophosphate (cAMP) levels in adipocytes
D. elevated acetyl-CoA levels in skeletal muscle
E. increased gluconeogenesis

Correct Answer: A
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
In fasting or diabetes, lipolysis predominates in adipocytes because of the inability of these cells to obtain glucose, which is normally used as a source of glycerol-3-phosphate. Glycerol-3-phosphate is necessary for the esterification of fatty acids into triacylglycerides. Circulating fatty acids become the predominant fuel source, and beta-oxidation in the liver becomes substantially elevated. This leads to an increased production of acetyl-CoA. Although gluconeogenesis is increased (choice E) in the liver as a result of the persistent elevation of glucagon levels, this pathway does not supply acetyl-CoA for the production of ketone bodies. The increased gluconeogenesis predisposes oxaloacetate and reduces (not increases, choice B) the flow of acetyl-CoA through the citric acid cycle. As a consequence, acetyl-

CoA is diverted to the formation of ketone bodies. The persistently elevated levels of glucagon also increase the levels of cAMP in responsive tissues, such as adipocytes (choice C). This effect in adipocytes leads to persistently increased release of fatty acids to the circulation. Since skeletal muscle lacks receptors for glucagon, there is no diabetes-mediated increase in muscle metabolism and thus no elevation in acetyl-CoA levels in skeletal muscle (choice D).

QUESTION 221
Control of the rate of translational initiation can be exerted at the level of the activity of the guanosine triphosphate (GTP)-binding and hydrolyzing initiation factor, eIF-2. The efficiency with which eIF-2 recycles between the active GTP-bound form and the inactive GDPbound form is controlled by the action of the initiation factor depicted as "Factor ?" in below figure. What is the identity of this factor?

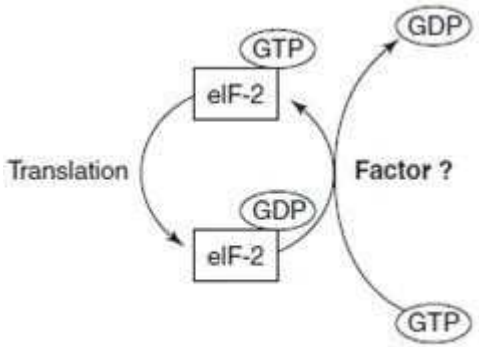


FIG. 3-1

A. eIF-1
B. eIF-2B
C. eIF-4A
D. eIF-4E
E. eIF-4G

Correct Answer: D
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
The eIF-2 cycle consists of the translation initiation factors, eIF-2A and eIF-2B (also called guanine- nucleotide exchange factor, GEF). The cycle involves the binding of GTP by eIF-2A forming a complex that then interacts with the initiator methionyl-tRNA. When the initiator methionyl-tRNA is placed into the correct position of the 40S ribosomal subunit, the GTP ishydrolyzed (generating GDP and release of Pi) to provide the energy necessary to correctly position the incoming mRNA such that the initiator AUG codon and the initiator methionyltRNA anticodon are aligned. In order to regenerate an active eIF-2A for subsequent translation initiation events, the GDP must be exchanged for GTP. The exchange reaction is catalyzed by eIF-2B. The initiation factor, eIF-1 (choice A), facilitates the correct

positioning of the initiator methionyl-tRNA and the mRNA. Initiation factor eIF-4A (choice C) binds to the mRNAand is required to "melt" any secondary structure that may exist at the 5'-end of the mRNA. Initiation factor eIF-4E (choice D) physically binds the cap structure at the 5'-end of the mRNA. Initiation factor eIF-4G (choice E) acts as a scaffold for eIF-4E facilitating cap structure binding by eIF-4E. Together, the complex composed of eIF-4A, eIF-4E, and eIF-4G is sometimes referred to as eIF-4F.

QUESTION 222
Fragile X syndrome is caused by expansion of a trinucleotide repeat in the fragile X mental retardation- 1 (FMR1) gene. This disorder is characterized by which of the following symptoms?

A. accumulation of copper leading to formation of Kayser-Fleischer rings in the eyes
B. hypoketotic hypoglycemia and metabolic acidosis
C. isovaleric acidemia, severe metabolic acidosis, and neonatal fatality
D. mental retardation of severity linked to the level of trinucleotide repeat expansion
E. very long-chain fatty acid accumulation and myelin defects

Correct Answer: D
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Fragile X syndrome is the most common form of inherited mental retardation. The symptoms of this disoder are caused by a disruption in the FMR1 gene. The disruption occurs as a result of the expansion of a trinucleotide repeat sequence in the 5' untranslated region of the FMR1 gene. The severity of mental retardation in fragile X syndrome is proportional to the level of expansion of the trinucleotide repeat. Copper accumulation leading to Kayser-Fleisher rings in the eyes(choice A) is indicative of Wilson disease, which results from impaired biliary copper excretion. The symptoms of hypoketotic hypoglycemia and metabolic acidosis (choice B) are indicative of glutaric acidemia type II, which results from deficiencies in mitochondrial ubiquinone oxidoreductase. Isovaleric academia (choice C) is a severe neonatal disorder resulting from a deficiency in one of the enzymes of branched-chain amino acid metabolism, isovaleryl- CoA dehydrogenase. Accumulation of abnormally high levels of very long-chain fatty acids and defects in myelin formation (choice E) are symptoms associated with X-linked adrenoleukodystrophy (X-ALD).

QUESTION 223
A 4-year-old patient is presented in the pediatric clinic with microcytic anemia. An analysis of his blood by nondenaturing electrophoresis reveals the following composition of hemoglobin isoforms:
HbF = 75%, HbA = 23%, HbA2 = 2%, and HbS = 0%. Using these data, is it possible to determine that the infant is most likely homozygous for which of the following?

A. complete deletion of the alpha-globin locus
B. complete deletion of the beta-globin locus
C. mutation in the promoter of the betaglobin genes
D. nonsense mutation in the alpha-globin genes

E. nonsense mutation in the beta-globin genes

Correct Answer: C
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
An individual with a normal profile of hemoglobin would have the largest percentage in the form of HbA reflecting normal expression from the alpha- and beta-globin genes. All individuals carry a small percentage (12%) of the fetal form, HbF, and the form which contains the -globin chains in place of the beta-globin of HbA. This latter hemoglobin is termed Hb . The increase in the level of the fetal

A_2

hemoglobin in this patient, along with the presence of a reduced level of the adult form, indicates that there is a defect in the ability to express normal levels of the beta-globin genes. This would be due to a promoter defect in the beta-globin gene. A complete deletion of the alpha-globin locus (choice A) leads to the condition known as hydrops fetalis and is incompatible with life. Complete loss of the beta- globin genes (choice B) results in the condition referred to as beta-thalassemia and there would be no HbA present in the blood. Nonsense mutations in the alphaglobin (choice D) or beta-globin (choice E) genes would result in phenotypes similar to those of gene deletions at these loci.

QUESTION 224
Hepatocytes deliver ketone bodies to the circulation because they lack which of the following enzymes?

A. beta-hydroxybutyrate dehydrogenase
B. hydroxymethylglutaryl-CoA-lyase
C. hydroxymethylglutaryl-CoA-synthetase
D. succinyl-CoA-acetoacetate-CoAtransferase
E. the form of the beta-ketothiolase necessary to hydrolyze acetoacetyl-CoA

Correct Answer: D
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Ketogenesis occurs in the liver from acetyl-CoA during high rates of fatty acid oxidation and during early starvation. The principal ketone bodies are acetoacetate and betahydroxybutyrate, which are reversibly synthesized in a reaction catalyzed by betahydroxybutyrate dehydrogenase. The liver delivers beta-hydroxybutyrate to the circulation where it is taken up by non-heptatic tissue for use as an oxidizable fuel. The brain will derive much of its energy from ketone body oxidation during fasting and starvation. Within extrahepatic tissues, beta-hydroxybutyrate is converted to acetoacetate by beta- hydroxybutyrate dehydrogenase. Acetoacetate is reactivated to acetoacetyl-CoA in a reaction catalyzed by succinyl-CoA-acetoacetate-CoA-transferase (also called acetoacetate: succinyl-CoA-CoA transferase),

which uses succinyl-CoA as the source of CoA. This enzyme is not present in hepatocytes. The acetoacetyl-CoA is then converted to 2 moles of acetyl-CoA by the thiolase reaction of fatty acid oxidation. Each of the other enzyme choices (A, B, C, and E) are found within hepatocytes.

QUESTION 225
Which of the following statements reflects the process by which the telomeric ends of chromosomes are replicated?

A. A unique RNA molecule serves as the primer for synthesis.
B. A unique RNA molecule serves as the template for synthesis.
C. Short template-independent block of DNA are ligated to the ends using a 5'-5' bond.
D. Telomeres are replicated as short tandem-repeated stretches of ribonucleotides instead of deoxyribonucleotides.
E. Telomeres are replicated in a templeindependent process.

Correct Answer: B
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
The telomeric end on the lagging strand of a replicating eukaryotic chromosomes are synthesized by an enzymatic activity termed telomerase. None of the other mechanisms (choices A, CE) represent the accurate replication of telomeres.

QUESTION 226
In carrying out an assay using cultured hepatocytes, you find that addition of hemin (Fe3+ heme) does not have the expected consequence of reduced protoporphyrin IX synthesis. This result suggests that your hepatocytes harbor a mutant form of one of the heme-regulated enzymes of porphyrin biosynthesis. Which of the following represents the likely enzyme?

A. ALA dehydratase
B. ALA synthase
C. ferrochelatase
D. heme oxygenase
E. PBG deaminase

Correct Answer: B
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
In the liver, hemin acts as a feedback inhibitor on ALAsynthase reducing its activity. In addition, hemin acts to repress transport of ALAsynthase into the mitochondria as well as repressing synthesis of the enzyme. Therefore, a continued synthesis of protoporphyrin IX in the presence of hemin indicates that ALA synthase is active but nonresponsive to the inhibitory action of hemin. None of the other enzymes of heme biosynthesis (choices A, CE) are inhibited by hemin.

QUESTION 227
Hemochromatosis, a disorder that is the result of excess iron accumulation, is caused by deficiencies in which of the following proteins?

A. divalent metal transporter-1 (DMT1)
B. human leukcocyte antigen (HLA) complex iron protein (HFE)
C. ferritin
D. ferroportin
E. transferrin

Correct Answer: B
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Hemochromatosis is defined as a disorder in iron metabolism that is characterized by excess iron absorption, saturation of iron-binding proteins, and deposition of hemosiderin in the tissues. The primary affected tissues are the liver, pancreas, and skin. Iron deposition in the liver leads to cirrhosis and in the pancreas causes diabetes. The excess iron deposition leads to bronze pigmentation of the organs and skin. In fact, the bronze skin pigmentation seen in hemochromatosis, coupled with the resulatant diabetes lead to the designation of this condition as bronze diabetes. The primary cause of hemochromatosis is the inheritance of an autosomal recessive allele. The locus causing hemochromatosis has been designated HFE and is a major histocompatibility complex (MHC) class-1 gene. The gene encodes an alpha-chain protein with three immunoglobulinlike domains. This alpha- chain protein associates with beta-2-microglobulin. Normal HFE has been shown to form a complex with the transferrin receptor and in so doing is thought to regulate the rate of iron transfer into cells. A mutation in HFE will therefore, lead to increased iron uptake and storage. The majority of hereditary hemochromatosis patients harbor a mutation in HFE that results in the substitution of Cys 282 for a Tyr. This mutation causes loss of conformation of one of the immunoglobulin domains in HFE. Another mutation found in HFE causes a change of His68 to Asp. DMT1 (choice A) is responsible for the intestinal absorption of dietary iron and thus, a deficiency in this protein would lead toreduced total body iron, not excess. Ferritin (choice C) is the intracellular iron binding and storage protein. A deficiency in ferritinwould lead to less iron deposition, not excess. Ferroportin (choice D) is the iron transport protein that moves dietary iron from within intestinal enterocytes across the basolateral membrane to the circulation, therefore, a deficiency in this protein would have consequences similar to deficiencies in DMT1. Transferrin (choice E) is the iron transport protein of the blood that binds to the trasferrin receptor on cell surfaces, allowing cellular uptake of circulating iron. A deficiency in this protein would lead to less iron deposition not more.

QUESTION 228
Amother has brought her 3-month-old baby to the pediatrician and indicates that the infant is lethargic and has poor suckling and seems uninterested in eating. In addition, the mother notes that the baby's diapers often smell like burnt sugar. This infant likely has a defect in which of the following enzymes?

A. branched-chain alpha-keto acid dehydrogenase
B. cystathionine synthase
C. glycine cleavage complex (GCC)
D. homogentisate oxidase
E. phenylalanine hydroxylase

Correct Answer: A
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
The symptoms exhibited by the infant are reflective of maple syrup urine disease (MSUD). This disease is caused by defects in branched-chain alpha-keto acid dehydrogenase, one of the enzymes used in the catabolism of the branched-chain amino acids (BCAAs) and the associated branched-chain alpha-keto acids (BCKAs). The classical symptom of this disease is the odor of burnt sugar in the diapers of afflicted infants. Left untreated, infants will die in the first few months of life from recurrent metabolic crisis and neurologic deterioration. Deficiency in cystathione synthase (choice B) manifests with elevated urine homocystine. The major sites of organ involvement are the CNS, the skeletal and vascular systems, and the eyes. The involvement of the vascular system leads to thromboembolism and is the major cause of death with cystathionine synthase deficiency. The GCC (choice C) is responsible for the catabolism of glycine to C , N ,+, and , -methylene-THF. Deficiency in the

O_2

GCC results in nonketotic hyperglycinemia. Deficiency in homogentisate oxidase (choice D) is the cause of alkaptonuria. Alkaptonuria is characterized by urine that turns brown on exposure to air. Deficiency in phenylalanine hydroxylase causes hyperphenylalaninemia (phenylketonuria, PKU). Newborn screening occurs in many countries including the United States and the disorder can be effectively treated with dietary intervention.

QUESTION 229
Amale infant, delivered at 38 weeks' gestation, presents with severe bowing of long bones, blue sclera, and craniotabes at birth. Radiographs show severe generalized osteoporosis, broad and crumpled long bones, beading ribs, and a poorly mineralized skull. Histologic examination of the long bones revealed the trabecula of the calcified cartilage with an abnormally thin layer of osteoid, and the bony trabeculae are thin and basophilic. The symptoms observed in the infant are characteristic of which disease?

A. Ehlers-Danlos syndrome
B. Marfan syndrome
C. occipital horn syndrome

D. osteogenesis imperfect
E. scurvy

Correct Answer: D
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Osteogenesis imperfecta consists of a group of at least four types (mild, extensive, severe, and variable). The disorder is characterized by brittle bones and abnormally thin sclerae, which appear blue owing to the lack of connective tissue. The symptoms arise due to defects in two alpha-collagen genes, the COL1A1 and COL1A2 genes. There have been over 100 mutations identified in these two genes. The mutations lead to decreased expression of collagen or abnormal pro1 proteins. The abnormal proteins associate with normal collagen subunits, which prevents the triple helical structure of normal collagen to form. Theresult is degradation of all the collagen proteins, both normal and abnormal. Ehlers-Danlos syndrome (choice A) comprises at least 10 defined types of a related disorder. Characteristic clinical features are easy bruising, markedly soft hyperextensible skin, extreme joint hypermobility, and the formation of thin, atrophic, "cigarette-paper" scarring following injury. Marfan syndrome (choice B) results in cardiovascular, musculoskeletal, and ophthalmic abnormalities. Hallmark clinical manifestations are aortic dilation, mitral valve prolapse, dissecting aneurysms, arachnodactyly, and ectopia lentis. Occipital horn syndrome (choice C), a disorder that manifests with symptoms similar to other collagen metabolism disorders, results from defects in copper metabolism. Clinical features include loose skin and joints, hernias, and abnormally shaped bones. Scurvy (choice E), which is caused by a deficiency in vitamin C, is characterized by decreased wound healing and hemorrhaging, anemia, osteoporosis, soft swollen gums, and easily bruised skin.

QUESTION 230
Obesity, genetic profile, and aging all contribute to the development of Type II diabetes. Of the following, which is the most important additive factor for these three conditions in the development of Type II diabetes?

A. elevated hepatic ketogenesis
B. elevated pancreatic glucagon secretion
C. impaired renal clearance of glucose
D. increased adipose tissue activity leading to hyperlipidemia
E. muscle resistance to insulin

Correct Answer: E
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
The influence of obesity, genetic profile, and age on overall metabolism is most significant at the level of skeletal muscle sensitivity to the actions of insulin (below figure). Due to the overall mass of skeletal muscle in the body, the uptake of glucose by this tissue, and consequently its role in blood glucose homeostasis, is a significant factor in insulin responses. Progressive loss of skeletal muscle sensitivity to insulin leads to increased rates of visceral cell lipolysis and pancreatic beta-

cell compensation. Eventually, the pancreas can no longer continue compensating for impaired insulin responses and pancreatic beta-cell decompensation occurs, further exacerbating the problem. The disrupted insulin response leads to increased hepatic gluconeogenesis, which further increases circulating glucose levels. The overall outcome of these reposnses is development of progressisely worsening Type II diabetes. Whereas, each of the other options (choices AD) will ensue due to impaired insulin responses in skeletal muscle, none is significant in the development of diabetes.

QUESTION 231
A2-month-old infant suffering from increased vomiting and diarrhea is seen in the hospital and observed to have significant abdominal distention due to hepatosplenomegaly. Unfortunately, the infant does not survive. Autopsy reveals calcification of the adrenals and massive accumulation of cholesteryl esters and triglycerides in most tissues. Analysis of enzyme activity in fibroblasts and lymphocytes demonstrates a significant acid lipase (cholesteryl ester hydrolase) deficiency. These clinical findings are indicative of which of the following disorders?

A. hyperlipoproteinemia, type I (familial liproprotein lipase deficiency)
B. I-cell disease (mucolipidosis type II)
C. Maroteaux-Lamy syndrome
D. Sanfilippo syndrome
E. Wolman disease

Correct Answer: E
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Wolman disease results from a deficiency in the lysosomal acid lipase enzyme (also called cholesteryl ester hydrolase) and is very nearly always a fatal disease of infancy. Symptoms of the disorder arise from massive accumulation of cholesteryl esters and triglycerides in most tissues. Clinical manifestations include hepatosplenomegaly leading to abdominal distention, GI abnormalities, steatorrhea, and adrenal calcification. Type I hyperlipoproteinemia (choice A) results from a deficiency in LPL activity. LPL is the enzyme found on the surface of vessel endothelial cells and is responsible for hydrolyzing fatty acids from the triglycerides found in circulating liporpotein particles. This action allows cells to get fatty acids for energy production from lipoproteins in the plasma. This disoder leads to massive accumulation of chylomicrons and triglycerides in the plasma. Symptoms associated with type I hyperlipoproteinemia are usually detected in childhood and include eruptive cutaneous xanthomatosis, hepatosplenomegaly, and repeated episodes of abdominal pain. I-cell disease (choice B) results from a deficiency in the targeting of lysosomal enzymes to the lysosomes. Affected cells have dense inclusion bodies filled with storage material, hence the derivation of the disease name. There are elevated levels of lysosomal enzymes in the plasma and body fluids of I-cell patients. Symptoms include severe psychomotor retardation, coarse facial features, and severe skeletal abnormalities. The rapidly progressing disease can lead to death between 5 and 8 years of age. Maroteaux- Lamy syndrome (choice C) results from a defect in the enzyme N-acetylgalactosamine-4-sulfatase (arylsulfatase B) responsible for the catabolism of complex glycosaminoglycans. There are three distinct forms of Maroteax-Lamy syndrome that range in severity. Symptoms include coarse facial features, skeletal abnormalities corneal clouding, and aortic valve disruption. Sanfillipo syndrome (choice D) comprises at least four distinct genetic defects that result from deficiencies in enzymes required for the catabolism of complex glycosaminoglycans of the heparan sulfate class. In all cases, the clinical symptoms are similar and include severe mental deterioration, hyperactivity, and disorders in the skin, lungs, heart, and skeletal muscle.

QUESTION 232
As a hypothetical approach to treating the hyperglycemia associated with Type II diabetes, a drug firm proposes to develop an inhibitor of liver glycogen

phosphorylase. What is the biochemical rationale for this approach to inducing hypoglycemia?

A. Hepatic fatty acid oxidation will decrease leading to reduced energy production needed for gluconeogenesis.
B. Hepatocytes will have a reduced capacity to store glucose following meals.
C. Liver glucose output will be reduced early during fasting.
D. The resultant increase in glycogen storage will inhibit glucose uptake by the liver, leading to increased usage in skeletal muscle.
E. There will be an increase in hepatic gluconeogenesis.

Correct Answer: C
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
During early fasting, as the level of glucose in the blood falls, the pancreas releases glucagon into the circulation to counter this drop. The major site of glucagon action is the liver. There it induces the activity of the glycogen phosphorylase leading to an increase in glucose release from glycogen stores. Thus, an inhibition of glycogen phsphorylase would limit the ability of the liver to provide glucose to the blood. Negatively affecting the activity of glycogen phosphorylase would not significantly affect the rate of hepatic fatty acid oxidation (choice A), skeletal muscle glucose usage (choice D), nor hepatic gluconeogenesis (choice E). The liver may have a reduced capacity for de novo storage of glucose following meals (choice B) due to a prior reduction in the release of glucose via the inhibition of glycogen phosphorylase; however, on fasting there would still be a reduction in glucose release.

QUESTION 233
Lipoprotein lipase (LPL) is the endothelial cellassociated enzyme necessary for release of fatty acids from circulating lipoproteins. Which of the following apolipoproteins is required to activate LPL- mediated release of fatty acids from chylomicrons?

A. apo A
B. apo
C. apo
D. apo CII
E. apo E

Correct Answer: D
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
The presence of apo CII on the surfaces of lipoprotein particles is necessary for the activation of endothelial cell LPL. Apo AI (choice A) activates LCAT. Apo (choice B) is derived via intestinal-

B_{48}

specific RNA editing and is exclusively a component of chylomicrons. Apo (choice C) and E

B_{100}

(choice E) are necessary for LDL interaction with the LDL receptor.

QUESTION 234
Which of the following is the hypophyseotropic hormone that regulates the activity of the lactotrophs of the anterior pituitary?

A. CRH
B. GnRH
C. growth hormone-releasing hormone (GRH)
D. prolactin-releasing factor (PRF)
E. thyrotropin-releasing hormone (TRH)

Correct Answer: D
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
The lactotrophs of the anterior pituitary secrete prolactin in response to the action of PRF. Corticotropin-releasing hormone, CRH (choice A) regulates primarily the secretion of ACTH, but also other products of the ACTH precursor protein, pro-opiomelanocortin, POMC. GnRH (choice B) controls the secretion of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) from the pituitary gonadotrophs. GRH (choice C) stimulates growth hormone secretion from pituitary somatotrophs. TRH (choice E) stimulates the thyrotropes to secrete thyroid-stimulating hormone, TSH (also called thyrotropin).

QUESTION 235
An individual harboring a mutation in ornithine transcarbamoylase (OTC) would be expected to exhibit which of the following measurable abnormalities?

A. citrullinemia
B. elevated urinary excretion of argininosuccinic acid
C. elevation in blood orotic acid
D. excess production of foam cells
E. uric acid deposition in the joints

Correct Answer: C
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
A deficiency in OTC results in one of the urea cycle defect diseases, which are the major causes of hyperammonemia in the newborn. Differentiation of which urea cycle enzyme is defective and causing the hyperammonemia can be accomplished by analysis of the levels of the various intermediates in the cycle (see below figure for UCD DDx).

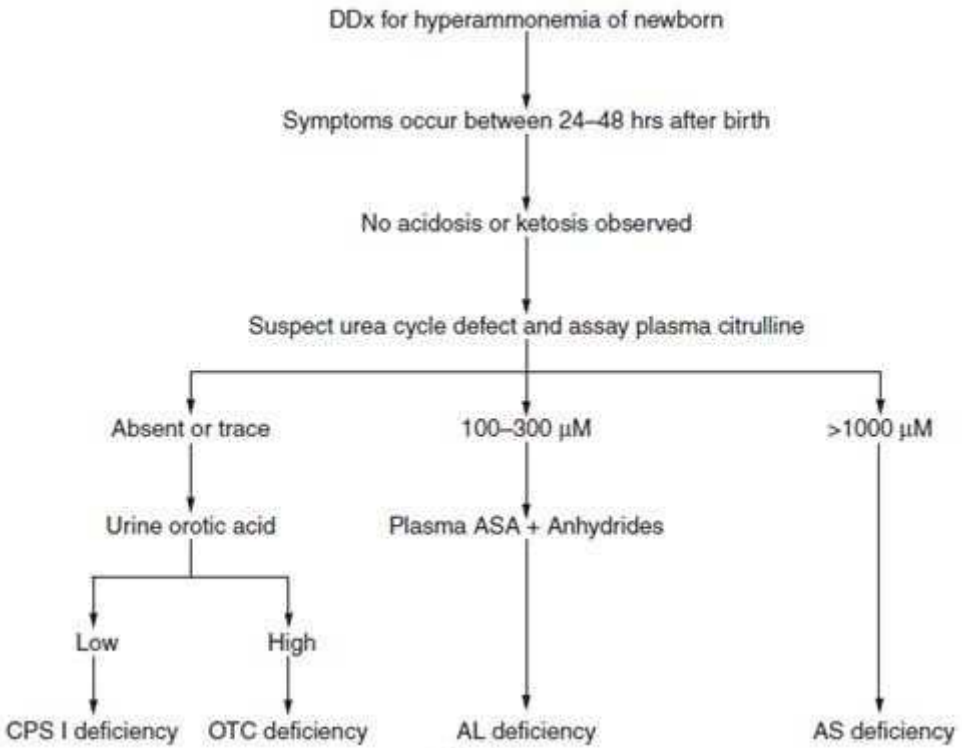


FIG. 3-6

Adefect in OTC prevents incorporation of carbamoylphosphate into ornithine (see below figure). The carbamoylphosphate will diffuse out of the mitochondria and serve as a precursor for the synthesis of the pyrimidine nucleotides in excess of need leading to an elevation of orotic acid (pyrimidine intermediate) in the blood. A deficiency of the urea cycle enzyme, ASD, will lead to citrullinemia (choice A). Elevation in excretion of argininosuccinate (choice B) will result from a deficiency in the urea cycle enzyme, arginosuccinase. Foam cells are lipidladen cells that are characteristic of disorders in lipid etabolism such as that seen in NPD, which is

caused by a deficiency in sphingomyelinase. Uric acid deposition (choice E) results from excess catabolism of the purine nucleotides.

QUESTION 236
You are examining the biochemical characteristics of the liver dysfunction in your patient, who is exhibiting signs of a glycogen storage disease. You have isolated the microsomal fraction (contains the endoplasmic reticulum) of a liver biopsy homogenate from your patient and a control individual for your studies. Incubation with radioactive phosphate-labeled glucose-6-phosphate results in an increase in isotope associated with the microsomes from your control sample but no increase in association with the microsomes from your patient. These results are best explained by a defect in which of the following?

A. glucose-6-phosphatase activity in the microsomes
B. microsomal glucose-6-phosphate transporter
C. cytosolic glucose-6-phosphatase
D. microsomal glucose transport
E. microsomal phosphate transporter

Correct Answer: B
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
The patient is suffering from von Gierke disease, which is glycogen storage disease type I. This disease results from one of several defects in the process of dephosphorylating glucose-6- phosphate to free glucose and the pathways are shown in below figure.

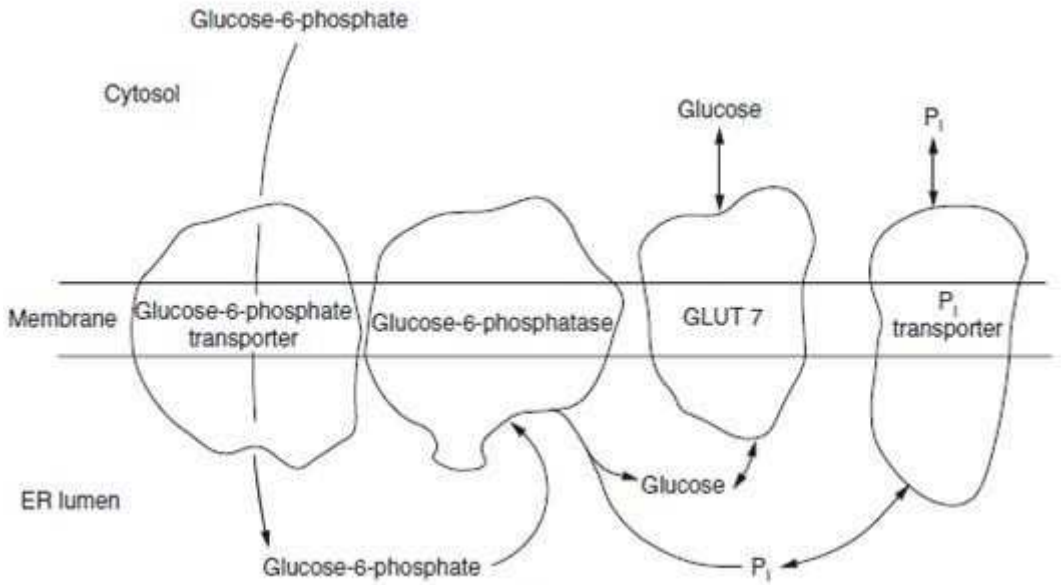


FIG. 3-12

The actual dephosphorylation takes place within the lumen of the ER where glucose-6-phosphatase resides, embedded in the membrane. Thus, glucose-6-phosphate must first be transported into the ER to be acted on by glucose- -phosphatase. Following dephosphorylation, the free glucose is then transported back out to the cytosol. In addition, the released inorganic phosphate (Pi) must also be transported to the cytosol. Because of this pathway and the multiple activities involved, there have been four distinct subtypes of this particular glycogen storage disease identified. Type Ia results from deficiencies in glucose-6-phosphatase, type Ib from deficiencies in the glucose-6-phosphate transporter, type Ic from deficiencies in the transporter, and type Id from deficiencies in GLUT7, which is the

P_i

glucose transporter in the membrane of the ER. When the ER is isolated (microsomal fraction) from cells and incubated with radiolabeld glucose-6-phosphate, there will be uptake of the label into the membranes only if the activity of the glucose-6-phosphate transporter is unaffected. Because the microsomes from the patient failed to take up the label, the data indicates the individual has a defect in the glucose-6-phosphate transporter and is suffering from type Ib glycogen storage disease. A deficiency in glucose-6-phosphatase (choice A) would not prevent uptake by the microsomes. Glucose- 6-phosphatase is not found in the cytosol (choice C). Deficiencies in the microsomal GLUT7 (choice D) or the Pi transporter (choice E) would lead to failure to take up the radio-labeled glucose.

QUESTION 237
Which of the following correctly defines the term: p ?

K_a

A. equilibrium constant for the dissociation of HA to and
B. ion constant of water
C. negative log of the concentration of
D. pH at which a molecule is neutrally charged
E. pH at which an equivalent distribution of acid and conjugate base exist in solution

Correct Answer: E
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
The term pKa defines the pH at which an equivalent distribution of acid and conjugate base (or base and conjugate acid) exists in solution. This term is derived from the equation demonstrating that pH = + log[ ]/[HA]. At the point of the dissociation where the concentration of the conjugate base [

pK_a

] is equal to that of the acid [HA] the value of [ ]/[HA] is equal to 1 and the log of 1 is 0,

A^-

therefore, at this point in a dissociation is equal to pH. The equilibrium constant for the

pK_a

dissociation of an acid (or base) is (choice A). The ion constant for water (choice B) is defined as

K_a

. The negative log of the hydrogen ion concentration [ ] (choice C) is pH. The pH at which a

K_w

molecule or compound is electrically neutral (choice D) is called the isoelectric point, pI.

QUESTION 238
Muscle membrane will depolarize in response to acetylcholine binding its receptors at the neuromuscular junction. Associated with this depolarization are changes

in glycogen metabolism in skeletal muscle cells. Which of the following represents the correct changes in enzyme activity seen in response to acetylcholine binding?

A. decreased glycogen phosphorylase kinase activity due to an increase in calcium binding to its calmodulin subunit
B. decreased phosphorylation of, and inhibited activity of glycogen phosphorylase kinase
C. increased glycogen phosphorylase kinase activity due to an activation of phosphoprotein phosphatase
D. increased glycogen phosphorylase kinase activity due to an increase in calcium binding to its calmodulin subunit
E. increased phosphorylation of, and inhibited activity of glycogen phosphorylase kinase

Correct Answer: D
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
The binding of acetylcholine to its receptor at the neuromuscular junction results in depolarization of the muscle membrane. This event triggers the release of calcium ions from the sarcoplasmic reticulum. The increase in intracellular calcium concentration leads to many changes in enzyme activity. One effect of calcium is that it is bound by various calciumregulated binding proteins. One of the subunits of glycogen phosphorylase kinase is calmodulin, a calcium-binding protein. The interaction of calcium with calmodulin alters the conformation of calmodulin, which leads to an activation of glycogen phosphorylase kinase activity in the absence of phosphorylation. The activity of glycogen phosphorylase kinase is increased not decreased (choice A) by calcium interaction with calmodulin present in the enzyme complex. Increases in intracellular calcium (as in response to acetylcholine binding at the neuromuscular junction) do not affect the level of phosphorylation of glycogen phosphorylase kinase (choices B and E) nor does it affect the activity of phosphoprotein phosphatase (choice C).

QUESTION 239
A 42-year-old man presents with hepatomegaly, jaundice, refractory ascites, and renal insufficiency. Peripheral leukocytes exhibit only 20% of normal glucocerebrosidase activity. Which of the following would explain his symptoms?

A. Fabry disease
B. Gaucher disease
C. Krabbe disease
D. Niemann-Pick disease type II C
E. Tay-Sachs disease

Correct Answer: B
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:

Numerous severe disorders are associated with the inability to properly degrade the complex carbohydrate moieties of glycosaminoglycans, proteoglycans, and glycoproteins. These disorders fall into a broad category of diseases termed the lysosomal storage diseases. Several of the lysosomal storage diseases result in hepatosplenomegaly, renal dysfunction, and skeletal defects, and therefore these symptoms are not diagnostic in themselves of a particular lysosomal storage disease, but only indicative of such disorders. However, disorders such as NPD (choice D) and Tay-Sachs disease (choice E) are of such severity that early childhood mortality occurs and thus would not present in a 42- year-old patient. It is necessary to evaluate enzyme function in skin fibroblasts or white cells of the blood. Gaucher disease is caused by a defect in glucocerebrosidase activity and hence an assayable decrease in the activity of this enzyme would be diagnostic of this disease. Fabry disease (choice A) results from a defect in alpha-galactosidase A. Krabbe disease (choice C) results from a defect in galactocerebrosidase. Based on genetic linkage analyses as well as enzyme studies and the characterization of accumulating lysosomal substances, NPD (choice D) should be divided into type I and type II; type I has two subtypes, A and B (NPA and NPB), which show deficiency of acid sphingomyelinase. NPD type II likewise has two subtypes, types C1 and C2 (NPC) and type D (NPD), both of which show accumulation of abnormal LDL-cholesterol. The NPC1 gene contains regions of homology to mediators of cholesterol homeostasis suggesting why LDL-cholesterol accumulates in lysosomes of afflicted individuals. Tay-Sachs disease (choice E) results from a defect in hexosaminidase A.

QUESTION 240
The parents of a 1-year-old boy are alarmed at the increasing frequency of their child biting his lips and finger tips. In addition, on several occasions they have noticed what appear to be particles of "orange sand" in their son's diapers. They report to their pediatrician that they believe their child is delayed in acquiring motor skills such as holding up his head and sitting unaided. Clinical tests performed on serum and urine indicate a threefold increase in serum uric acid and a tenfold elevation in the urinary ratio of uric acid to creatinine. These findings are suggestive of which of the following disorders?

A. adenosine deaminase deficiency
B. adenylosuccinate lyase deficiency
C. Lesch-Nyhan disease
D. purine nucleotide phosphorylase deficiency
E. orotic aciduria

Correct Answer: C
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Deficiencies in the purine nucleotide salvage enzyme, HGPRT, cause three overlapping clinical syndromes. The most severe deficiency (patients having less than 1.5% residual enzyme activity) results in debilitating neurologic disability, overproduciton of uric acid, and behavioral abnormalities that include impulsive and self-injurious activities such as biting finger tips and lips. This severe form of HGPRT deficiency is referred to as Lesch-Nyhan disease. The overproduction of uric acid leads to symptoms of gout and the appearance of "orange sand" in the urine. Deficiencies in ADA (choice A), another purine nucleotide salvage enzyme, are the cause of severe-combined immunodeficiency syndrome, SCID. SCID is characterized by a lack of both cell-mediated and humoral immunity. ADSL (choice B) is an enzyme in the pathway of de novo purine nucleotide synthesis. It is also an important component of the purine nucleotide cycle (see below figure). Deficiencies in ADSLcause psychomotor retardation, epileptic seizures, growth retardation, and muscle wasting. Deficiencies in PNP (choice D) result in a form of immunodeficiency characterized by defective cell-mediated responses. Afflicted individuals may also have normal, hyperactive, or reduced humoral immunity. Orotic aciduria is caused by deficiencies in the de novo pathway of pyrimidine nucleotide synthesis. Adeficiency in either of the last two enzymes in the pathway, orotate phosphoribosyltransferase or OMP decarboxylase, leads to orotic aciduria.

QUESTION 241
The ability of the liver to regulate the level of blood glucose is critical for survival. Anumber of sources of carbon atoms of nonhepatic origin are used by the liver for gluconeogenesis. However, the net conversion of carbons from fat into carbons of glucose cannot occur in humans because of which of the following?

A. Fat oxidation occurs in the mitochondria and gluconeogenesis occurs in the cytosol.
B. States of catabolism and anabolism are never concurrently active.
C. Storage of fats occurs in adipose tissue and gluconeogenesis occurs in liver and kidney.
D. The carbons of acetyl-CoA from fat oxidation are lost as C in the TCA cycle.
E. The carbons of acetyl-CoA from fat oxidation inhibit conversion of pyruvate to oxaloacetate.

Correct Answer: D
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
When the carbons of fatty acids are oxidized for energy production, the by-product of that process is the two-carbon compound, acetyl-CoA. Acetyl-CoA can then enter the TCA cycle for complete oxidation. Although, several compounds of the TCA cycle can be directed into the gluconeogenic pathway of glucose synthesis, the carbons of acetyl-CoA cannot provide a net source of carbon in that latter pathway. This is due to the fact that, following entry of the two carbons of acetyl-CoA into the TCA cycle, two carbons are lost as CO_2 during the subsequent reactions of the cycle. The subcellular compartmentalization of fat oxidation and gluconeogenesis (choice A) has no bearing on net carbon deposition into glucose. Anabolic and catabolic reactions (choice B) are always occuring concurrently in cells but at different rates dependent on cellular status. The site of fat storage (choice C) has no bearing on net incorporation of carbon into glucose. Acetyl-CoA does not inhibit conversion of pyruvate to oxaloacetate (choice E) but acts as an allosteric activator of pyruvate carboxylase, a gluconeogenic enzyme.

QUESTION 242
Endothelial cells respond to certain stimuli by inducing the conversion of arginine to citrulline leading to the activation of a signaling cascade that involves which of the following?

A. adenylate cyclase
B. guanylate cyclase
C. phosphatidylinositol-3-phosphate kinase (PI3K)
D. PLC-gamma
E. protein kinase C (PKC)

Correct Answer: B
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Certain endothelial cell-stimulating signals, such as vasodilators, induce the production of NO during the conversion of arginine to citrulline via a reaction catalyzed by nitric oxide synthase (NOS). When NO is produced, it passes out of the endothelial cells and enters the underlying smooth muscle cells. Within smooth muscle cells, NO reacts with the heme moiety of a soluble guanylyl cyclase, resulting in activation of the latter and a consequent elevation of intracellular levels of cGMP. The net effect is the activation of cGMP-responsive enzymes, which lead to smooth muscle cell relaxation. None of the signaling enzymes or molecules (choices A, CE) are involved in the NO-mediated signaling cascade.

QUESTION 243
The metabolic pathway depicted in below figure is critically important as a means of energy production in skeletal muscle cells. Which of the following correctly identifies this pathway?

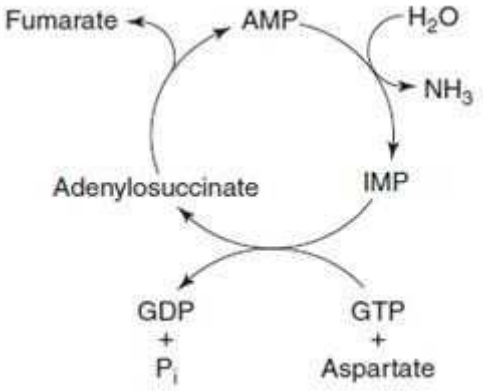


FIG. 3-2

A. ADA cycle
B. hypoxanthine-guanine phosphoribosyltransferase (HGPRT) cycle
C. nonoxidative cycle in pentose phosphate pathway
D. purine nucleotide cycle
E. urea cycle

Correct Answer: D
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:

The synthesis of AMP from IMP and the salvage of IMP via AMP catabolism have the net effect of deaminating aspartate to fumarate. This process has been termed the purine nucleotide cycle. This cycle is very important in muscle cells. Increases in muscle activity create a demand for an increase in the TCA cycle, to generate more NADH for the production of ATP. However, muscle lacks most of the enzymes of the major anapleurotic reactions. Muscle replenishes TCA cycle intermediates in the form of fumarate generated by the purine nucleotide cycle. There is no HGPRT or ADA cycle and hence, choices Aand B do not represent valid options. Choices C and E constitute pathways that do not involve nucleotides.

QUESTION 244
During the process of protein synthesis, the factor eEF-2 induces the hydrolysis of GTP. The energy of this hydrolysis is coupled to which of the following?

A. amino acid activation by attachment to a tRNA
B. correct alignment of the mRNA on the 40S ribosome
C. formation of the 80S initiation complex
D. formation of the peptide bond
E. translocation of the ribosome

Correct Answer: E
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
The translation factor, eEF-2, is involved in the process of peptide elongation. Specifically, eEF-2 catalyzes the GTP-dependent translocation of the ribosomes along the mRNA to the next codon. Attachment of an amino acid to a tRNA (choice A) is catalyzed by the family of aminoacyl-tRNA synthetases. Alignment of the mRNA on the 40S ribosome (choice B) is facilitated by the initiation factor eIF-1. Formation of the 80S initiation complex (choice C) occurs after complete assembly of the 40S preinitiation complex and requires the activity of eIF-5. Formation of the peptide bond (choice D) occurs through the action of peptidyltransferase.

QUESTION 245
Patients with poorly controlled diabetes mellitus have elevated levels of blood glucose. One severe consequence of the hyperglycemia is an increase in glucose attachment to serum proteins. Which of the following proteins, when glycosylated, is an excellent measure of the length of time someone has suffered from an episode of hyperglycemia?

A. albumin
B. cholesterol
C. fatty acids
D. hemoglobin
E. transferrin

Correct Answer: D
Section: Biochemistry

Explanation

Explanation/Reference:
Explanation:
The formation of glycosylated hemoglobin occurs spontaneously (i.e., nonenzymatically through a reaction known as the Amadori rearrangement) in red blood cells. The amino terminal groups of the beta-chains of hemoglobin complex with the aldehyde groups of glucose to form an amino ketone linkage. This form of hemoglobin is known as Hb . Measurement of the circulating level of

A_{1c}

glycosylated hemoglobin is a diagnostic tool used to determine the relative length of hyperglycemia and can be used as a measure of treatment effectiveness. Glucose does not form covalent bonds with any of the other choices (A, B, C, and E).

QUESTION 246
The ability of rod cells in the eye to respond to light and transmit that response to the optic nerve requires that the 11-cis form of vitamin A be attached to which of the following proteins?

A. cGMP phosphodiesterase
B. Na+ channel
C. rhodopsin
D. scotopsin
E. transducin

Correct Answer: D
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Both rod and cone cells contain a photoreceptor pigment in their membranes. The photosensitive compound (photoreceptor) of most mammalian eyes is a complex of protein and an aldehyde form of vitamin A. The protein component is a member of the opsin family called scotopsin. The photoreceptor of rod cells is specifically called rhodopsin (choice C) or visual purple, which is a complex between the protein scotopsin and the 11-cis-retinal form of vitamin A. Intracellularly, rhodopsin is coupled to a specific G-protein called transducin (choice E). When the rhodopsin is exposed to light it is bleached releasing the 11-cis-retinal from opsin. Absorption of photons by 11-cis-retinal triggers a series of conformational changes on the way to conversion all-trans-retinal. The release of opsin results in a conformational change in the photoreceptor. This conformational change activates transducin, leading to an increased GTP-binding by the alpha-subunit of transducin. Binding of GTP releases the alpha- subunit from the inhibitory beta- and gamma-subunits. The GTPactivated alpha-subunit in turn activates an associated phosphodiesterase (choice A), an enzyme that hydrolyzes cyclic-GMP (cGMP) to GMP. Cyclic GMP is required to maintain the Na+ channels (choice B) of the rod cell in the open conformation. The drop in cGMP concentration results in complete closure of the Na+ channels.

QUESTION 247

In an assay for the presence of a specific disease gene alelle in several individuals, you isolate genomic DNA from each and perfom polymerase chain reaction (PCR) using gene-specific primers. The PCR product is expected to have a recognition site for the restriction endonuclease BamHI. Following PCR and BamHI digestion, the products are separated by gel electrophoresis and the results are shown in below figure. Which lane corresponds to the individual demonstrating heterozygosity for the BamHI site?

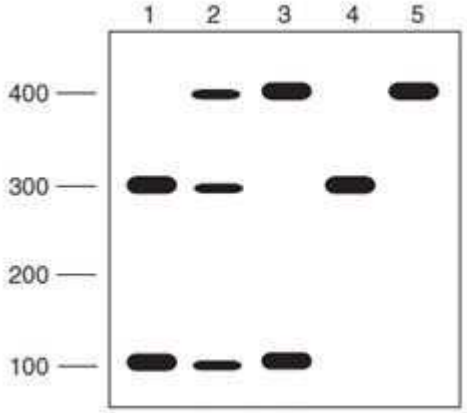


FIG. 3-3

A. 1
B. 2
C. 3
D. 4
E. 5

Correct Answer: B
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Someone who exhibits heterozygosity would harbor two distinct alelles. In the case of this analysis, they would be identified as containing a copy of the gene that does not harbor the BamHI site and a copy that does harbor the site. The presence of the BamHI site in the PCR product in this example would result in the generation of 300 and 100 bp fragments. The lack of the site would yield a product of 400 bp. Thus, following PCR amplification and BamHI digestion of DNA from a heterozygote, one would be able to observe three bands of equal intensity. A person who was homozygous for having the BamHI-containing sequence would result in two bands (choice A) whose intensities would be greater than the three of the heterozygote. A person homozygous for the lack of the BamHI site would yield a single 400 bp band (choice D). The banding patterns observed in lanes 3 (choice C) and 5 (choice E) would not be possible from this analysis.

QUESTION 248
Which of the following symptoms can occur frequently in infants suffering from mediumchain acyl- CoA dehydrogenase (MCAD) deficiency if periods between meals are protracted?

A. bone and joint pain and thrombocytopenia
B. hyperammonemia with decreased ketones
C. hyperuricemia and darkening of the urine
D. hypoglycemia and metabolic acidosis with normal levels of ketones
E. metabolic alkalosis with decreased bicarbonate

Correct Answer: D
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
In infants, the supply of glycogen lasts less than 6 hours and gluconeogenesis is not sufficient to maintain adequate blood glucose levels. Normally, during periods of fasting (in particular during the night) the oxidation of fatty acids provides the necessary ATP to fuel hepatic gluconeogenesis as well as ketone bodies for nonhepatic tissue energy production. In patients with MCAD deficiency there is a drastically reduced capacity to oxidize fatty acids. This leads to an increase in glucose usage with concomitant hypoglycemia. The deficit in the energy production from fatty acid oxidation, necessary for the liver to use other carbon sources, such as glycerol and amino acids, for gluconeogenesis further exacerbates the hypoglycemia. Normally, hypoglycemia is accompanied by an increase in ketone formation from the increased oxidation of fatty acids. In MCAD deficiency there is a reduced level of fatty acid oxidation, hence near normal levels of ketones are detected in the serum. None of the other choices (A, B, C, and E) reflect symptoms related in any way to MCAD deficiency and are not in themselves indicative of any specific disorder per se.

QUESTION 249
Reticulocytes control the rate of globin synthesis as a consequence of the level of heme in the cell. This prevents globin protein from being made when there are insufficient amounts of heme. Which of the following best explains the effects of heme on protein synthesis in these cells?

A. A heme-controlled phosphatase dephosphorylates cap-binding factor, which prevents recognition of globin mRNA by the ribosomes.
B. A tRNA-degrading enzyme is active in the absence of heme.
C. Heme normally activates peptidyltransfersase in reticulocytes.
D. RNA polymerase activity is decreased in reticulocytes by low heme.
E. The initiation factor eIF-2 becomes phosphorylated, reducing its level of activity.

Correct Answer: E
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
One mechanism by which initiation of translation in eukaryotes is effected is by phosphorylation of a ser(S) residue in the alphasubunit of eIF-2. The factor eIF-2 requires activation by interaction with GTP. The energy of GTP hydrolysis is used during translational initiation, thereby allowing eIF-2 to have GDP bound instead of GTP. In order to reactivate eIF-2, the GDP must be exchanged for GTP. This requires an additional protein of the GEF family known as eIF-2B. The phosphorylated form of eIF-2, in the absence of the eIF-2B, is just as active an initiator of translation as the nonphosphorylated form. However, when eIF-2 is phosphorylated, the GDP-bound complex is stabilized and exchange for GTP is inhibited. When eIF-2 is phosphorylated, it binds eIF-2B more tightly thus slowing the rate of exchange. It is this inhibited exchange that affects the rate of initiation. Within reticulocytes the phosphorylation of eIF-2 is the result of an activity called heme-controlled inhibitor, HCI (see below figure).

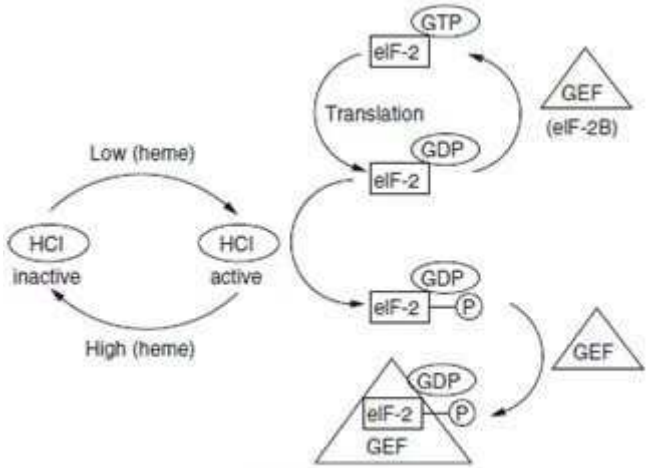


FIG. 3-13

The presence of HCI was first seen in an in vitro translation system derived from lysates of reticulocytes. When heme is limiting it would be a waste of energy for reticulocytes to make globin protein, since active hemoglobin could not be generated. Therefore, when the level of heme falls, HCI becomes activated, leading to the phosphorylation of eIF-2 and reduced globin synthesis. Removal of phosphate is catalyzed by a specific eIF-2 phosphatase which is unaffected by heme. There is no heme- controlled phosphatase activity (choice A) in any cell. No tRNA-specific degrading enzymes (choice B) are present in cells. There is no effect of heme levels on peptidyltransferase activity (choice C) or RNA polymerase activity (choice D).

QUESTION 250
Infants exhibiting profound metabolic ketoacidosis, muscular hypotonia, developmental retardation, and who have very large accumulations of methylmalonic acid in their blood and urine suffer from a disorder known as methylmalonic acidemia. This disorder results from a defect in which of the following enzymes?

A. alpha-keto acid dehydrogenase
B. homogentisic acid oxidase
C. methylmalonyl-CoA mutase

D. phenylalanine hydroxylase
E. tyrosine aminotransferase

Correct Answer: C
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Defects in methylmalonyl-CoA mutase activity comprise four distinct genotypes whose clinical symptoms are remarkably similar. Characteristic findings in methylmalonyl-CoA mutase deficiency include failure to thrive leading to developmental abnormalities, recurrent vomiting, respiratory distress, hepatomegaly, and muscular hypotonia. In addition, patients have severely elevated levels of methylmalonic acid in the blood and urine. Unaffected individuals have near undetectable levels of methylmalonate in their plasma, whereas, affected individuals have been found to have levels ranging from 3 to 40 mg/dL in their blood. Deficiency in alpha-ketoacid dehydrogenase (choice A) results in MSUD, so named because of the characteristic odor of the urine in afflicted individuals. Mental retardation in the MSUD is extensive. Deficiency in homogentisic acid oxidase (choice B) results in alkaptonuria. Alkaptonuria results from the accumulation of homogentisic acid, a byproduct of tyrosine catabolism, in the urine and tissues. Oxidation of homogentisate in the urine causes it to turn dark and in the tissues results in ochronosis, which refers to the ochre color of the deposits in connective tissue, bones, and other organs. Deficiency in phenylalanine hydroxylase (choice D) results in PKU which results in severe mental retardation if not detected and treated properly. Deficiency in tyrosine aminotransferase (choice E) results in eye, skin, and neurologic symptomology. The neurologic symptoms are similar to those seen in PKU.

QUESTION 251
Following a minor respiratory illness, a seemingly healthy, developmentally normal 15-month-old boy exhibited repeated episodes of severe lethargy and vomiting following periods of fasting, such as during the middle of the night. The parents brought the infant to the emergency room following a seizure. The child was hypoglycemic and was administered 10% dextrose, but remained lethargic. Blood ammonia was high, liver function tests were slightly elevated, and his serum contained an accumulation of dicarboxylic acids. Only low levels of ketones were detecteable in the urine. This infant suffers from which of the following disorders?

A. glutaric acidemia type II
B. Lesch-Nyhan syndrome
C. MCAD deficiency
D. pyruvate dehydrogenase (PDH) deficiency
E. type III (Cori) glycogen storage disease

Correct Answer: C
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Deficiency in MCAD is the most common inherited defect in the pathways of mitochondrial fatty acid oxidation. The most common presentation of infants with this disorder is episodic hypoketotic hypoglycemia following periods of fasting. Although the first episode may be fatal, and incorrectly ascribed to sudden infant death

syndrome, patients with MCAD deficiency are normal between episodes and are treated by avoidance of fasting and treatment of acute episodes with intravenous glucose. Accumulation of acylcarnitines (dicarboxylic acids) is diagnostic, in particular octanoylcarnitine. Glutaric acidemia type II (choice A) results from a defect in electron transfer flavoproteinubiquinone oxidoreductase and presents with symptoms of hypoketotic hypoglycemia as in the case of MCAD deficiency. However, this disorder manifests within the first 2448 h after birth and is frequently associated with congenital anomalies. Lesch-Nyhan syndrome (choice B) results from a defect in HGPRT--an enzyme involved in nucleotide metabolism. Symptoms of Lesch-Nyhan syndrome include hyperuricemia, bizarre neurobehavioral manifestations, growth retardation, and anemia. Deficiency in PDH (choice D) results in lactic acidemia, which can be quite severe at birth leading to neonatal fatality. Milder deficiency results in lactic acidemia associated with profound psychmotor retardation. Cori disease (choice E) results from a defect in the glycogen debranching enzymes. Clinical features include hepatomegaly, hypoglycemia, skeletal myopathy and short stature, and cardiomyopathy.

QUESTION 252
A 28-year-old man has the following symptoms: diffuse grayish corneal opacities, anemia, proteinuria, and hyperlipemia. Renal function is normal and serum albumin level is only slightly elevated. Plasma triglycerides and unesterified cholesterol levels are elevated, as are levels of phosphatidylcholine. These symptoms are indicative of which lipoproteinassociated disorder?

A. Bassen-Kornzweig syndrome
B. familial hypercholesterolemia (FH)
C. familial hypertriacylglycerolemia
D. familial lecithin-cholesterol acyltransferase (LCAT) deficiency
E. Wolman disease

Correct Answer: D
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Two familial syndromes directly involve defects in LCAT. Familial LCAT deficiency is characterized by near complete absence of the enzyme activity from the plasma. Fish eye disease is characterized by an absence of LCAT activity toward high-density lipoproteins (HDLs) but presence of activity toward LDLs. Clinical features of familial LCAT deficiency include corneal opacities, anemia, and proteinuria. Due to the lack of LCAT activity, the plasma level of esterified cholesterol is lower than normal and phosphatidylcholine (the principal source of fatty acid for esterification to cholesterol) levels are higher than normal. The profile of all classes of plasma lipoproteins in patients with familial LCAT deficiency is abnormal. Bassen-Kornzweig syndrome (choice A), also identified as abetalipoproteinemia, is due to a defect in apo B expression. Clinical symptoms include retinitis pigmentosa, ataxic neuropathy, and erythrocytes that appear thorny (acanthocytosis). FH (choice B) is characterized by reduced LDL clearance, which leads to severe hypercholesterolemia. Major clinical symptoms are arterial deposition of LDL-cholesterol, which leads to atherosclerosis and coronary artery disease. Deposition of LDL- cholesterol is also seen in tendons and skin resulting in xanthomas. Familial hypertriacylglycerolemia (choice C), also identified as hyperlipoproteinemia type IV, is a form of LPL deficiency. The defect leads to increased levels of circulating VLDLs and is associated with glucose intolerance and hyperinsulinemia. This disorder is frequently associated with Type II diabetes. Wolman disease (choice E) is cholesterol ester storage disease that leads to massive accumulation of cholesteryl esters and triglycerides in most tissues. This disease is almost always fatal within the first year of life and thus would not be present in a 28-year-old.

QUESTION 253
A 23-year-old man sees his physician to ask about the recent appearance of several large closely spaced bumps on his elbows. Suspecting that these are fatty

eruptions, the physician tests the man's blood for lipid, cholesterol, and lipoprotein levels. Results show elevated cholesterol and triglycerides and the presence of a variant form of very low-density lipoprotein (VLDL) identified as beta-migrating VLDL (-VLDL). Amore careful analysis of the biochemical properties of the apoproteins associated with the beta-VLDL particles identifies a form of apo E that has a more negative charge than apo E from normal individuals. These results indicate the individual is afflicted with which of the following hyperlipoproteinemias?

A. type I (familial LPL deficiency)
B. type II (FH)
C. type III (dysbetalipoproteinemia)
D. type IV (familial hypertriglycerolemia)
E. Wolman disease

Correct Answer: C
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Familial dysbetalipoproteinemia (type III hyperlipoproteinemia) results from a genetic variant in the apo E gene that causes poor interaction of chylomicron remnants and VLDLs with the apo E receptor. This results in the presence, in the serum, of beta-migrating VLDL (- VLDLs), which are cholesterol- rich remnants of both intestinal chylomicrons and hepatic VLDL. Diagnosis of type III hyperlipoproteinemia is indicated by elevated plasma cholesterol and triglyceride, xanthomas (fatty eruptions under the skin), and of course the presence of -VLDL. Type I hyperlipoproteinemia (choice A) results from defects in the activity or activation of LPL and results in the massive accumulation of chylomicrons in the plasma. The disease is usually detected in childhood following recurrent attacks of abdominal pain, hepatosplenomegaly, and pancreatitis. Familial hypercholesterolemia (choice B) is the result of defects in the LDL receptor. The defects lead to characteristic elevation in LDL, deposition of LDL-derived cholesterol in the tendons and skin and in the arteries. Individuals homozygous for defective LDL receptors have severe hypercholesterolemia (6501000 mg/dL) and coronary heart disease begins early in childhood with death caused by myocardial infarct before the age of 20. Type IV hyperlipoproteinemia (choice D) is associated with overproduction VLDLs. An associated glucose intolerance and hyperinsulinemia are also seen in this disorder. Wolman disease (choice E) is caused by a deficiency in lysosomal acid lipase and results in massive accumulation of cholesteryl esters and triglycerides in most tissues. The disease is almost always fatal before the age of 1 year.

QUESTION 254
I-cell disease (also identified as mucolipidosis type II) is characterized by the presence of inclusion bodies in fibroblasts (hence the derivation of the term I-cell), severe psychomotor retardation, corneal clouding, and dystosis multiplex. These symptoms arise from a defect in the targeting of lysosomal enzymes due to an inability to carry out which of the following processes?

A. produce mannose-6-phosphate modifications in lysosomal enzymes
B. recycle the lysosomal receptor for mannose-6-phosphate present on lysosomal enzymes
C. remove mannose-6-phosphates from lysosomal enzymes prior to their transport to the lysosomes
D. synthesize the mannose-6-phosphate receptor found in lysosomes
E. transport mannose-6-phosphate receptors to lysosomes

Correct Answer: A
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Enzymes that are destined for the lysosomes (lysosomal enzymes) are directed there by a specific carbohydrate modification. During transit through the Golgi apparatus a residue of Nacetylglucosamine- 1-phosphate is added to carbon 6 of one or more specific mannose residues that have been incorporated into these enzymes. The N-acetylglucosamine is activated by coupling to UDP and is transferred by an Nacetylglucosamine phosphotransferase yielding N-acetylglucosamine-1- phosphate-6-mannoseprotein. A second reaction removes the Nacetylglucosamine leaving mannose residues phosphorylated in the sixth position. Aspecific mannose-6-phosphate receptor is present in the membranes of the Golgi apparatus. Binding of mannose-6-phosphate to this receptor targets proteins to the lysosomes. Defects in the proper targeting of glycoproteins to the lysosomes can also lead to clinical complications. Deficiencies in N-acetylglucosamine phosphotransferase lead to the formation of dense inclusion bodies in fibroblasts. Two disorders related to deficiencies in the targeting of lysosomal enzymes are termed I-cell disease (mucolipidosis II) and pseudo-Hurler polydystrophy (mucolipidosis III). I-cell disease is characterized by severe psychomotor retardation, skeletal abnormalities, coarse facial features, painful restricted joint movement, and early mortality. Pseudo- Hurler polydystrophy is less severe; it progresses more slowly, and afflicted individuals live to adulthood. Each of the other choices (B, C, D, and E) represent other potential pathways that are not affected in the processing, delivery, or presentation of lysosomal enzymes or the receptors that recognize the properly processed enzymes.

QUESTION 255
A30-month-old child presents with coarse facial features, corneal clouding, hepatosplenomegaly, and exhibiting disproportionate short-trunk dwarfism. Radiographic analysis indicates enlargement of the diaphyses of the long bones and irregular metaphyses, along with poorly developed epiphyseal centers. Other skeletal abnormalities typify the features comprising dystosis multiplex. The child's physical stature and the analysis of bone development indicate the child is suffering from which of the following disorders?

A. Hunter syndrome
B. Hurler syndrome
C. Maroteaux-Lamy syndrome
D. Morquio syndrome type B
E. Sanfilippo disease type A

Correct Answer: B
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Although multiorgan involvement, liver and spleen enlargement, and skeletal abnormalities are common to all the mucopolysaccharidotic (MPS) diseases, each encompasses features that allow for specific diagnosis. Hurler syndrome is characterized by progressive multiorgan failure and premature death. Hallmark features include enlargement of the spleen and liver, severe skeletal deformity, and coarse facial features (which are associated with the constellation of defects referred to as dystosis multiplex). The disease results from a defect in alpha-L-iduronidase activity, which leads to intracellular accumulations of heparin sulfates and dermatan

sulfates. The accumulation of these GAGs (glycosaminoglycan) in Hurler syndrome patients severely affect development of the skeletal system leading, primarily, to defective long bone growth plate disruption. Hunter syndrome (choice A) hasfeatures similar to that of Hurler with a lack of corneal clouding. Additionally, symptoms progress slower, with onset of symptoms occurring between 2 and 4 years of age. Maroteaux-Lamy syndrome (choice C) encompasses symptoms similar to Hurler but with normal mental development. Morquio syndrome (choice D) comprises two related disorders, both of which are characterized by short-trunk dwarfism, fine corneal deposits, and a skeletal dysplasia (spondyloepiphyseal) distinct from other MPS. Sanfilippo syndrome (choice E) comprises four recognized types characterized by severe CNS degeneration with only mild involvement of other organ systems. Symptoms do not appear until 26 years of age.

QUESTION 256
Loss of the hepatic protein hepcidin can lead to severe iron overload with symptoms resembling those of hemochromatosis. Which of the following functions of hepcidin accounts for the iron overload when the protein is deficient?

A. activates the expression of the ironresponse element-binding protein that regulates transferring receptor and ferritin mRNA translation
B. decreases the level of intestinal membrane iron transporters, resulting in reduced iron uptake
C. facilitation of the interaction of transferring with the transferrin receptor
D. forms a complex with ferritin allowing for higher intracellular storage
E. promotes the formation of hemosiderin, thus detoxifying iron

Correct Answer: B
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Hepcidin is a hepatically synthesized iron regulatory protein that functions by inhibiting the presentation of one or more of the iron transporters [e.g., DMT1 and Ireg1 (ferroportin)] in intestinal membranes. With a high iron diet, the level of hepcidin mRNA increases and conversely its levels decrease when dietary iron is low. This is occurring simultaneous to reciprocal changes in the levels of the transporters proteins themselves. Loss of hepcidin activity would then lead to unregulated iron uptake from the intestines leading to iron overload. In fact, it is now considered that defects in hepcidin function contribute to the development of hemochromatosis. Hepcidin does not activate expression of iron-response elementbinding protein (choice A), facilitate transferring interaction with the transferring receptor (choice C), form a complex with ferritin (choice D), nor promote the formation of hemosiderin (choice E).

QUESTION 257
In an enzyme with a critical Glu residue in the active site, which of the following amino acid substitutions would be expected to have the least effect on enzyme activity?

A. Arg
B. Asp
C. Lys
D. Ser
E. Tyr

Correct Answer: B
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Glutamic acid is an acidic amino acid at physiologic pH and therefore, substitution for another acidic amino acid, such as aspartic acid, would be expected to have minimal effect on the activity of the enzyme. Arginine (choice A) and lysine (choice C) are both basic amino acids at physiologic pH and would not be able to substitute for an acidic amino acid. Serine (choice D) and tyrosine (choice E) both have ionizable hydroxyl groups but the pKa values of those hydroxyl groups would not favor substitution for an acidic amino acid.

QUESTION 258
Many proteins undergo modifications during and/or following translation. The ATPdependent polyubiquitination of proteins is a signal for which of the following events?

A. addition of the oligosaccharide core to the N-linkage site adjacent to the ubiquitin
B. recognition by the toxin of diphtheria
C. recycling of the protein back to the endoplasmic reticulum (ER) from the cis-Golgi to allow proper folding
D. targeting the protein for degradation in the proteosome
E. translocation of the protein into the nucleus

Correct Answer: D
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
The ATP-dependent poly-ubiquitination of proteins is a signal that the protein is misfolded and thus, needs to be targeted by the proteosome for degradation. Mono-ubiquitination is known to initiate cell signaling by allowing other proteins that contain ubiquitin-binding domains to interact with the mono- ubiquitinated substrate. Mono-ubiquitination has also been associated with targeting of membrane proteins to the lysosome. None of the other examples (choices AC, E) are associated with addition of ubiquitin.

QUESTION 259
Some viruses, for example, poliovirus, contain a protease that cleaves one of the eukaryotic initiation factors allowing for cap-independent translational initiation of viral RNAs at internal ribosome entry site (IRES). Which of the following factors is the target of these viral proteases?

A. eIF-2
B. eIF-2B
C. eIF-4A

D. eIF-4E
E. eIF-4G

Correct Answer: E
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Eukaryotic viral RNAs are not capped and the host 40S ribosome interacts with these viral RNAs at an IRES. Capped eukaryotic mRNAs are recognized by the complex of eIF- 4E and eIF-4G, which in turn allows for interaction of the 40S ribosome with the mRNA (see below figure).

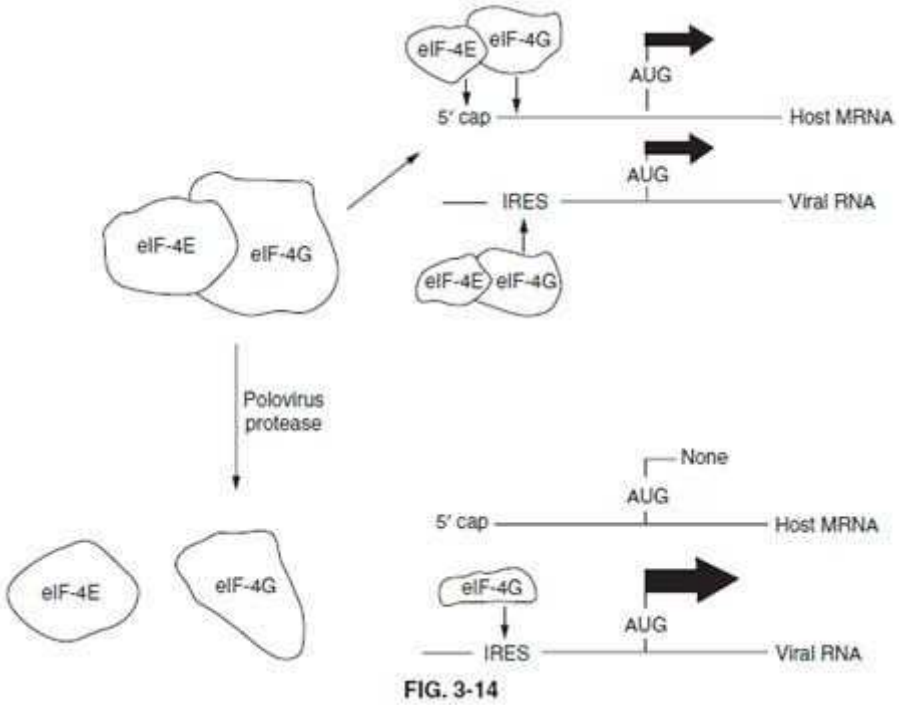


FIG. 3-14

Initiation factor eIF-4E physically binds the cap structure in eukaryotic mRNAs and this function is facilitated by interaction of eIF-4E with eIF-4G. Thus, loss of the interaction of eIF-4E with the protease cleaved eIF-4G results in loss of translational initiation from capped mRNAs. However, the binding of 40S ribosomes to viral RNAs does not require eIF-4E, only eIF-4G. The protease encoded by the poliovirus cleaves the eIF-4E binding site on eIF-4G. None of the other translation factors (choices AC, E) are targets for poliovirus protease.

QUESTION 260
A 37-year-old man presents with tophaceous deposits within the articular cartilage, synovium, tendons, tendon sheaths, pinnae, and the soft tissue on the extensor surface of the forearms. These clinical observations suggest the patient is suffering from which of the following disorders?

A. ADA deficiency
B. gout
C. Lesch-Nyhan syndrome
D. purine nucleoside phosphorylase(PNP) deficiency
E. von Gierke disease

Correct Answer: B
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Gout is characterized by elevated levels of uric acid in the blood and urine. Uric acid is the end-product of purine catabolism and excess production results from a variety of metabolic abnormalities that lead to overproduction of purines via the de novo pathway. Uric acid is very insoluble and when generated in large amounts will precipitate as uric acid crystals in the joints of the extremities and in renal interstitial tissue. These deposits are gritty or sandy in nature and thus are termed tophaceous deposits. ADA (choice A) and PNP (choice D) deficiencies result in various degrees of immune dysfunction and are not associated with gouty episodes. Lesch-Nyhan disease (choice C) is due to loss of HGPRT activity. Characteristic symptoms include severe mental retardation and self-mutilation. A much less severe symptom associated with Lesch-Nyhan disease is hyperuricemia, which leads to gouty episodes. However, other symptoms are of such severity that patients die very early in life. Deficiency in glucose-6-phosphatase results in von Gierke disease (choice E). Clinical symptoms of von Gierke disease include fasting hypoglycemia, lactic acidemia, and mild gouty episodes. The hyperuricemia of von Gierke disease is seldom severe enough to lead to the level of gouty deposits observed in this patient.

QUESTION 261
The initial reaction of the de novo synthesis pathway for pyrimidine nucleotides begins with glutamine and C and is complete with the formation of uridine monophosphate. Which of the following

O_2

represents the ratelimiting enzyme in this pathway?

A. aspartate transcarbamoylase
B. orotate monophosphate decarboxylase
C. phosphoribosylpyrophosphate (PRPP) amido transferase
D. PRPP synthetase

E. ribonucleotide reductase

Correct Answer: A
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
The first reaction of de novo pyrimidine biosynthesis is catalyzed by ATC. This reaction is also the rate-limiting step in this pathway. OMP decarboxylase (choice B) catalyzes the decarboxylation of OMP, yielding UMP. PRPP amido transferase (choice C) is an enzyme of the de novo purine biosynthesis pathway. PRPP synthetase (choice D) catalyzes the production of PRPP (used in the synthesis of purines and pyrimidines) from ribose-5-phosphate and ATP. Ribonucleotide reductase (choice E) is required for the reduction of ribonucleotides to deoxyribonucleotides.

QUESTION 262
One important function of nitric oxide (NO) is the induction of vascular smooth muscle relaxation in response to acetylcholine. The production of NO requires which amino acid?

A. arginine
B. asparagines
C. cysteine
D. glutamine
E. lysine

Correct Answer: A
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
NO is generated from arginine in a reaction catalyzed by NOS. The other product of the reaction is citrulline. None of the other amino acids (choices B, C, D, and E) are substrates for NOS.

QUESTION 263
In renal insufficiency, calcium absorption is reduced and leads to increased bone resorption, a condition referred to as renal osteodystrophy. Treatment with which of the following can assist in the amelioration of the symptoms of this condition?

A. antidiuretic hormone
B. calcitonin
C. calcitriol

D. growth hormone
E. parathyroid hormone

Correct Answer: C
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Calcitriol [1,25-(OH -D] is the hormonally active form of vitamin D and functions in concert with

$)_2$

PTH and calcitonin to regulate serum calcium and phosphorous levels. The major function of calcitriol is the induction of synthesis of an intestinal calcium-binding protein, calbinden, which facilitates intestinal absorption of calcium. Oral administration of calcitriol will increase intestinal calcium uptake, but the hormone does not enter the peripheral circulation in significant amounts. Therefore, patients with renal osteodystrophy may need intravenous administration of calcitriol. Antidiuretic hormone (choice A) is responsible for renal water readsorption in response to increased extracellular Na+ concentrations, which lead to increased plasma osmolarity. Calcitonin (choice B) acts to block bone resorption when there are sufficient levels of calcium in the serum. Growth hormone (choice D) does not influence calcium homeostasis and would therefore not be useful in the treatment of renal osteodystrophy. PTH (choice E) acts to increase bone resorption, in concert with calcitriol, when serum calcium levels fall.

QUESTION 264
A 32-year-old woman is diagnosed with hypertension, hypernatremia, hypokalemia, and alkalosis. Measurements of plasma glucocorticoid levels show them to be within the normal range; however, renin and angiotensin II levels are suppressed. Ultrasound indicates the possible existence of an adrenal cortical mass. These symptoms are likely due to excess production of which of the following hormones?

A. aldosterone
B. androstenedione
C. dehydroepiandrosterone (DHEA)
D. estradiol
E. testosterone

Correct Answer: A
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Primary aldosteronism (Conn syndrome) leads to elevated production of aldosterone and the symptoms presented by the patient. This disorder is due to small adenomas of the glomerulosa cells of the kidney. The associated hyperkalemia, hypertension, and hypernatremia lead to a reduction in renin release from the

juxtaglomerulosa cells. Renin is required for the conversion of angiotensinogen (released from the liver) to angiotensin I (which is in turn converted to angiotensin II by converting enzyme), and so reduced levels of renin lead to reduced levels of angiotensin II. Androstenedione (choice B) is produced from pregnenolone via the 17alpha-hydroxylase pathway of androgen synthesis in the adrenal cortex or of estrogen synthesis in the ovary. Androstenedione is derived from DHEA(choice C) and is converted to estradiol (choice D) in the ovary or to testosterone (choice E) in the testis. Estrogens are responsible for maturation of the ovaries and testosterone maturation of sperm. None of these steroids regulate sodium or potassium and would therefore not lead to the symptoms presented if elevated or reduced.

QUESTION 265
The anticancer drug, Taxol, has been an effective chemotherapeutic agent in the fight against ovarian cancer. Which of the following represents the mechanism of action of Taxol?

A. binds to the activated form of the RAS protein, which in turn interferes with the signaling cascades involving this protein
B. binds to microtubules, which stabilizes them preventing their shortening and interfering with cell division
C. interacts with the tumor supressor protein (pRB) encoded by the retinoblastoma susceptibility gene inducing its suppressive activity
D. interacts with topoisomerase II preventing its role in DNA synthesis, which effectively terminates replication
E. interferes with steroid hormone receptor interaction with DNA, thus preventing the growth induction by this class of hormone

Correct Answer: B
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
The compound paclitaxel (the generic name for Taxol) interferes with the normal function of microtubule growth leading to increased stability of the structure. This effect of Taxol destroys the cell ability to use its cytoskeleton in a flexible manner. Specifically, Taxol binds to the tubulin protein of microtubules and locks them in place. The resulting microtubule/Taxol complex does not have the ability to disassemble. This adversely affects cell function because the shortening and lengthening of microtubules (termed dynamic instability) is necessary for their function as a transportation highway for the cell. Chromosomes, for example, rely on this property of microtubules during mitosis. Therefore, the inability of cells to organize and undertake the necessary movements of mitosis prevents cell division. Since cancer cells are rapidly proliferating cells, the action of Taxol inhibits their growth. None of the other choices (A, CE) reflect the actions of Taxol on cells.

QUESTION 266
A 17-year-old man who reports to his physician that he is incapable of obtaining an erection is also quite embarrassed by the apparent enlargement of his breasts (gynecomastia). These symptoms, when present in males, are associated with an excessive production of which of the following hormones?

A. corticotropin-releasing hormone
B. GnRH
C. growth hormone
D. melanocyte-stimulating hormone
E. prolactin

Correct Answer: E
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Prolactin is necessary for initiation and maintenance of lactation. Physiologic levels act only on breast tissue primed by female sex hormones. Endocrine dysfunction leading to excessive prolactin production is associated with breast enlargement and impotence in males. Excessive production of corticotropin-releasing hormone (choice A) would result in an increase in adrenocorticotropic hormone (ACTH) production, which would lead to enhanced glucocorticoid and mineralocorticoid production. Excessive production of GnRH (choice B) would lead to increased production of luteinizing hormone (LH), follicle-stimulating hormone (FSH), and chorionic gonadotropin (hCG), with consequent effects on the female reproductive system. Excessive production of growth hormone (choice C) leads to gigantism if it occurs prior to epiphysial plate closure. If excessive release occurs following epiphysial plate closure acromegaly results, with characteristic facial changes (protruding jaw, enlarged nose) and enlarged feet, hands, and skull. Excessive production of melanocyte-stimulating hormone (choice D) would lead to hyperpigmentation of the skin.

QUESTION 267
Numerous inherited disorders are the result of the expansion of trinucleotide (triplet) repeats either within the coding regions of genes or the untranslated regions of the resultant RNAs. Which of the following diseases has been shown to be caused by triplet expansion?

A. cystic fibrosis (CF)
B. Duchenne muscular dystrophy (DMD)
C. FH
D. Huntington disease (HD)
E. Menkes disease

Correct Answer: D
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
HD is an autosomal-dominant disorder leading to progressive memory loss, personality changes, and peculiar motor problems such as involuntary movements of the arms and legs. The disease results from the expansion of a CAG triplet in the amino terminus of the HD protein, referred to as huntingtin. The triplet repeat number ranges from 10 to 30 on the normal chromosome and from 36 to 121 on the HD chromosome. There is a general correlation between the length of the repeat and the age of onset of symptoms. CF (choice A) is primarily due to a common mutation (in 70% of cases) that deletes three nucleotides in exon 10 of the CF gene, which codes for the CF transmembrane conductance receptor (CFTR). Over 600 other mutations have been identified in the CF gene. DMD (choice B) results from deletions in one or more of the exons of the DMD gene, which encodes the protein referred to as dystrophin. FH (choice C) results from defects in the gene encoding the LDL receptor. These defects encompass insertions and deletions that can be found throughout the length of the LDLreceptor gene. Menkes disease (choice E) is due to defects in copper absorption leading to defective function of numerous enzymes that need copper as a cofactor.

QUESTION 268
Correct targeting of newly synthesized hydrolytic enzymes to the lysosomes requires which of the following modifications?

A. attachment of mannose-6-phosphate to the enzymes
B. gamma-carboxylation of glutamate residues in the enzymes
C. O-linkage of carbohydrate to the enzymes
D. prenylation of the enzymes
E. proteolytic activation following transport to the lysosome

Correct Answer: A
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Enzymes that are targeted to the lysosomes undergo a specific two-step modification in the Golgi complex. The first step in the modification involves the attachment of an alpha- acetylglucosamine 1- phosphate residue to the six position of a mannose residue on the high man-nose carbohydrate portion of lysosomal enzymes. The second step involves removal of the N-acetylglucosamine residue exposing the mannose-6-phosphate marker. The presence of mannose-6-phosphate is necessary for targeting lysosomal enzyme to the lysosomes and deficiencies in the enzyme responsible for the first reaction in the modification lead to severe developmental abnormalities. Carboxylation of glutamate residues (choice B) is necessary to the function of several enzymes of the coagulation cascades. Lysosomal enzymes are not modified by attachment of carbohydrate through O-linkage (choice C). Many membraneanchored proteins undergo lipid modification by prenylation (choice D) such as the protein product of the protooncogene RAS. Although many enzymes are activated by proteolytic processing (choice E), this is not required for targeting lysosomal enzymes to the lysosome.

QUESTION 269
When dividing cells are progressing through the cell cycle, many checks are imposed to ensure that the process is occuring with fidelity. A critical checkpoint in the cell cycle occurs in response to DNA damage, such as that induced by ultraviolet light. Which of the following cellcycle proteins is involved in DNA damagemediated cell-cycle arrest?

A. CDK2
B. cyclin A
C. cyclin D
D. E2F
E. p53

Correct Answer: E
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
The p53 protein is a tumor suppressor whose function is to ensure that cells with damaged DNAdo not progress through the cell cycle until that damage is repaired. The major response to p53 action is an increase in the expression of the p2 gene. Progression through the cell cycle requires, among other

1^{CIP}

activities, the concerted action of cyclins and cyclin-dependent kinases (CDKs) of which there are several. The activity of the CDKs is dependent on interaction with cyclins. However, the presence of CDK inhibitory proteins, CIPs, results in inhibition of the activity of CDKs. CIPs bind and inhibit CDK1, 2, 4, and 6 complexes. Thus, an increase in the activity of p53, which occurs in response to DNAdamage, results in a block to cell-cycle progression. The activity of CDK2 (choice A) is regulated by the presence of cyclin A. The cyclins (choice B and C) are regulators of the kinase activity of the CDKs. The transcription factor E2F (choice D) is regulated by interaction with the retinoblastoma susceptibility protein, pRB.

QUESTION 270
Severe combined immunodeficiency disease (SCID) is characterized by a complete lack of cell- mediated and humoral immunity. This disorder results from a deficiency in which of the following enzymes?

A. adenosine deaminase
B. asparatate transcarbamoylase
C. HGPRT
D. orotic acid decarboxylase
E. purine nucleotide phosphorylase

Correct Answer: A
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
ADA catalyzes the deamination of adenosine to inosine during the catabolism of purines. Loss of ADAleads to significantly elevated levels of phosphorylated deoxyadenosine (in particular deoxyadenosine triphosphate, dATP). Levels of dATP in ADA deficiency can reach 50 times normal. High concentrations of dATP inhibit ribonucleotide reductase, which is required for the generation of deoxynucleotides from ribonucleotides. The inhibition of ribonucleotide reductase leads to severely impaired cellular DNA synthesis. Since lymphocytes must be able to proliferate dramatically in response to antigenic challenge, the loss of ADA activity results in a near complete lack of immune function. ATC (choice B) is a component of a multifunctional enzyme, which catalyzes the rate- limiting reaction of pyrimidine biosynthesis. No known deficiencies in this enzyme have been identified, likely due to the embryonic lethality predicted if the enzyme were defective. HGPRT (choice C) catalyzes the salvage of hypoxanthine to IMP and guanine to GMP. Deficiency in HGPRT results in Lesch-Nyhan syndrome. Orotic acid decarboxylase (choice D) catalyzes the decarboxylation of OMP to UMP. Deficiency in this enzyme results in orotic aciduria, type II. PNP (choice E) is also a purine catabolic enzyme, which converts inosine to hypoxanthine and guanosine to guanine. Deficiency in PNP leads to a mild immunodeficiency.

QUESTION 271

The forensic analytical technique identified as DNA fingerprinting refers to which of the following processes?

A. the establishment of a complete collection of cloned fragments of DNA
B. the identification of sequences of DNA to which specific proteins bind, thereby rendering them resistant to digestion by DNA-degrading nucleases
C. the specific association of complimentary strands of DNA to one another
D. the synthetic oligonucleotide-directed enzymatic amplification of specific sequences of DNA
E. the use of repeat sequences to establish a unique pattern of fragments for any given individual

Correct Answer: E
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
DNAfingerprinting refers to the process of using polymorphic repeat sequences to establish a unique pattern of DNA fragments for any given individual. The polymorphic repeats that are identifiable by the fingerprinting technique are hypervariable repeats such as variable number tandem repeats (VNTRs). The bands are detected by Southern blotting enzyme-digested chromosomal DNA and probing the blot with various different VNTR probes. The generation of a DNA library (choice A) refers to the establishment of a complete collection of cloned fragments of DNA, either from genomic sources or cDNA. DNA footprinting (choice B) refers to the identification of sequences of DNA to which specific proteins bind, thereby rendering the DNA at that site resistant to digestion by DNA degrading nucleases. Hybridization (choice C) refers to the specific association of complimentary strands of DNA to one another. The PCR technique (choice D) uses synthetic oligonucleotides to direct the enzymatic amplification of specific sequences of DNA.

QUESTION 272
Glucagon binding to liver cells induces an increase in intracellular cAMP concentration. The rate- limiting step in cholseterol biosynthesis is regulated as a consequence of this glucagon-mediated rise in cAMP. The effect of increased cAMP on the rate of cholesterol biosynthesis occurs because of which of the following?

A. AMP-activated protein kinase (AMPK) is activated and directly phosphorylates human menopausal gonadotropin (HMG)-CoA reductase, leading to an increase in the activity of the latter enzyme.
B. Cyclic AMP-dependent protein kinase (PKA) is activated and directly phosphorylates HMG-CoA reductase, reducing the activity of the latter enzyme.
C. PKA is activated and phosphorylates AMP-regulated kinase, which then phosphorylates and activates HMGCoA reductase.
D. Removal of phosphate from HMG-CoA reductase increases its activity. Activated PKA results in a reduced level of phosphate removal from HMG-CoA reductase so that the latter enzyme is kept less active.
E. The increased cAMP directly inhibits HMG-CoA reductase.

Correct Answer: D
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Regulation of HMG-CoAreductase (the ratelimiting enzyme of cholesterol biosynthesis) activity is complex and involves a number of distinct enzyme activities (below figure).

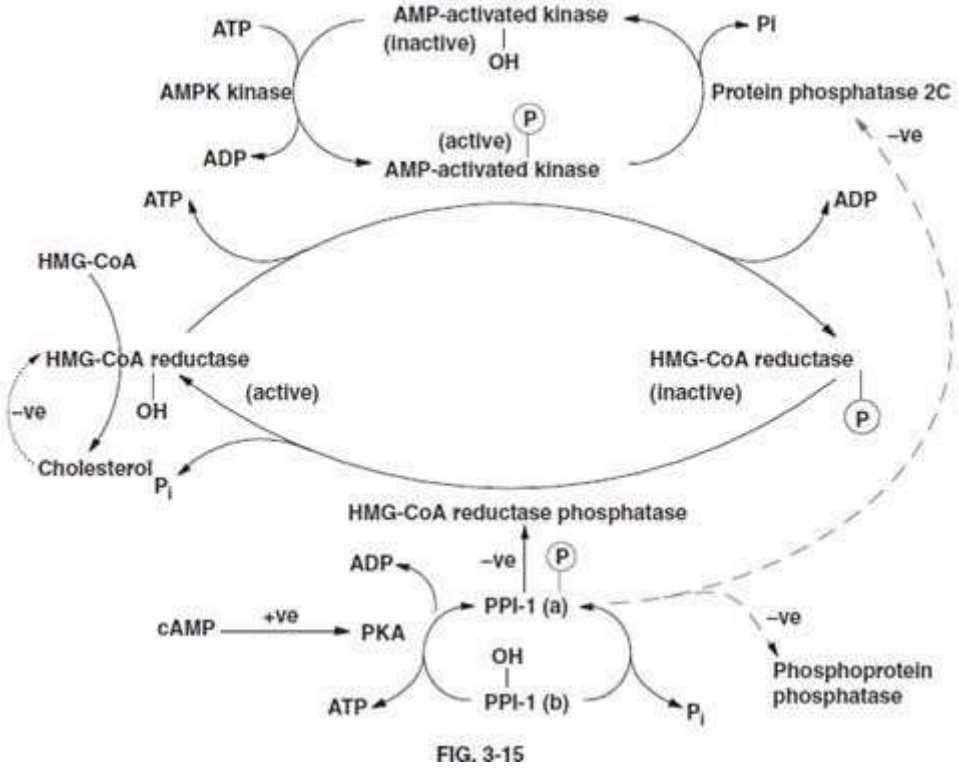


FIG. 3-15

Since cholesterol biosynthesis consumes large amounts of energy, it needs to be regulated in response to energy demands, particularly in hepatocytes. The principal site for the action of the hypoglycemic response hormone, glucagon, is the liver. Glucagon binding to hepatocytes triggers the liver to stop catabolizing carbohydrate and to divert carbon atoms into the gluconeogenesis pathway. This change in hepatic metabolism, in response to glucagon, comes about through a change in the phosphorylation state of numerous enzymes. One of these enzymes is HMG-CoA reductase. HMG-CoA reductase is most active when in the nonphosphorylated state. The enzyme is phosphorylated and rendered less active through the action of AMP-regulated kinase. AMP levels rise as the energy charge in the cell declines and thus the cell is able to recognize this change, at the level of HMG-CoA reductase activity, by inducing its phosphorylation and inhibition. In order to reverse the effect of HMG-CoA phosphorylation the phosphates must be removed. This occurs through the action of HMG-CoA reductase phosphatase. HMGCoAreductase phosphatase is regulated through the action of protein phosphatase inhibitor-1 (PPI-1). In turn the activity of PPI-1 is regulated by its state of phosphorylation; it is more active when phosphorylated. When glucagon binds to hepatocytes, the result is a glucagon receptormediated activation of adenylate cyclase, which in turn produces cAMP from ATP. The effect of cAMP is to activate cAMP-dependent protein kinase which then phosphorylates a number

of substrates. With respect to glucagon-mediated regulation of cholesterol metabolism, PKA phosphorylates PPI-1. Phosphorylated PPI-1 is more active at inhibiting HMG-CoA reductase phosphatase so that the removal of phosphate from HMG-CoA reductase is inhibited. This keeps HMG-CoA reductase in the phosphorylated and less active state. AMPK is not directly affected by glucagon-mediated increases in the levels of cAMP (choice A). Although glucogon action leads to an increase in PKA activity, the latter enzyme does not itself phosphorylate HMG-CoA reductase (choice B). The activity of AMP-regulated kinase is affected by its level of phosphorylation but it is not phosphorylated by PKA(choice C). Cyclic AMPitself does not have a direct effect on HMG- CoAreductase (choice E).

QUESTION 273
You are tending to a patient with a high tendency to bleed. He bruises easily and has bleeding from his gums. Analysis of coagulation factors in his blood shows normal levels of factor V but low levels of factor VIII. Injection of factor VIII provides only minimal benefit and you find that the injected protein is rapidly degraded. Using a platelet aggregation test, you find that combination of your patient's serum with normal platelets results in only 20% of the platelet aggregation seen with both samples from a normal individual. Based on these findings, you determine that your patient is deficient in which of the following factors of coagulation?

A. factor X
B. factor XII
C. fibrinogen
D. thrombin
E. von Willebrand factor

Correct Answer: E
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
The von Willebrand factor is associated with subendothelial connective tissue and serves as a bridge between platelet glycoprotein GPIb/IX and collagen. This activity ensures that platelets can adhere to the exposed subendothelial surfaces at the site of tissue injury. In addition, von Willebrand factor and factor VIII exist in a noncovalently bound complex in the plasma. The interaction of factor VIII and von Willebrand factor greatly stabilizes factor VIII. For example, following infusion of factor VIII into patients with hemophilia A (caused by loss of factor VIII) the protein exhibits a serum halflife of around 12 hours. Conversely, when infused into patients with severe von Willebrand disease, VWD (lack of von Willebrand factor), the half-life of factor VIII is less than 2 hours. Therefore, individuals suffering from VWD will also have significantly reduced levels of circulating factor VIII. This fact results in the observation that patients with VWD exhibit symptoms of both platelet dysfunction and hemophilia. Deficiency in any of the other coagulation factors (choices AD) would not result in decreased stability of factor VIII observed as a reduction in circulating levels of this protein.

QUESTION 274
A 3-month-old infant exhibits profound neurologic deficit in addition to being blind and deaf. Pathologic examination indicates renal cysts, hepatomegaly, and facial dysmorphism. Biochemical analysis reveals plasma accumulations of very long-chain fatty acids, abnormal intermediates of bile acid synthesis, and a marked deficiency of plasmalogens. These physical and biochemical features are characteristic of which of the following disorders?

A. hyperpipecolic acidemia

B. infantile Refsum disease
C. neonatal adrenoleukodystrophy
D. rhizomelic chondrodysplasia punctata (RCDP)
E. Zellweger syndrome

Correct Answer: E
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Zellweger syndrome is the most severe of a group of diseases that result from defective assembly of the peroxisomes, leading to the characteristic symptoms observed in the patient. This syndrome is apparent at birth and leads to death within the first year. The cause of Zellweger syndrome is a failure to import newly synthesized peroxisomal proteins into peroxisomes. Hyperpipecolic academia (choice A), infantile Refsum disease (choice B), and neonatal adrenoleukodystrophy (choice C) are all much less severe disorders of the group that result from peroxisome dysfunction. Affected individuals with these latter disorders can survive into the third or fourth decade, albeit with deficits in vision, hearing, and cognitive function. It is suspected that the reduced severity of these three disorders, relative to Zellweger, relates to retention of partial gene function as opposed to complete loss. RCDP (choice D) is related to peroxisomal dysfunction at the level of their distribution and structure. The phenotype of RCDP differs from that of Zellweger syndrome in that patients have striking shortening of the proximal limbs, coronal clefts of vertebral bodies, and severely abnormal endochondrial bone formation.

QUESTION 275
Which of the following apoproteins is found exclusively associated with chylomicrons?

A. apo A
B. apo B48
C. apo CII
D. apo D
E. apo E

Correct Answer: B
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Apo is found exclusively associated with chylomicrons and no other lipoprotein particle. Apo

B_{48}

is synthesized from an mRNA that is transcribed from the apo gene. Following

B_{48}

transcription, the mRNA is edited within the intestinal epithelium yielding the apo transcript.

B_{48}

ApoA. (choice A) is an apoprotein found disulfide bonded to apo . This then forms a complex

B_{100}

with LDL, generating a novel lipoprotein particle identified as lipoproteinA., LpA.. LpA. has a strong resemblance to plasminogen and its presence in the circulation is highly correlated with premature coronary artery disease. Apo CII (choice C) is present in chylomicrons, VLDLs, LDLs, IDLs, and HDLs and is necessary for the activation of endothelial cell LPL. Apo D (choice D) is found exclusively with HDLs and is also associated with cholesterol ester transfer protein (CETP) activity. Apo E (choice E) is found in chylomicrons, VLDLs, LDLs, IDLs, and HDLs. It is necessary for interaction of lipoprotein with the LDL-receptor (which is also referred to as the apo /apo E

B_{100}

receptor).

QUESTION 276
A 9-month-old infant who suffered bouts of jaundice and was diagnosed with severe nonhemolytic icterus shortly after birth has died of kernicterus. During the periods of jaundice, serum analysis showed an increased concentration of indirect-reacting bilirubin with no detection of conjugated bilirubin. The premature death and early clinical findings in this infant suggest which of the following disorders?

A. AIP
B. Crigler-Najjar syndrome, type I
C. Dubin-Johnson syndrome
D. Gilbert syndrome
E. Rotor syndrome

Correct Answer: B
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:

Jaundice is caused by an elevation in the circulating levels of bilirubin, the heme degradation by- product. Bilirubin, which is toxic, is rendered harmless by binding to albumin in the serum and by conjugation to glucuronate in the liver. Profound hyperbilirubinemia leads to encephalopathy (kernicterus), which results in death if untreated. The hepatic conjugation of bilirubin to glucuronate is catalyzed by bilirubin-UDP-glucuronyltransferase (UGT). The conjugated form of bilirubin is less toxic due to its increased solubility. Hyperbilirubinemia can be of two types, unconjugated or conjugated. Defects in UGT will lead to unconjugated hyperbilirubinemia. The deficiency of UGT in Crigler-Najjar syndrome type I is complete (due to loss of coding exons in the UGT gene) and as a consequence affected individuals will die from the profound kernicterus. AIP (choice A) results from a defect in the activity of the porphyrin biosynthetic enzyme, PBG deaminase. This disorder results in neurovisceral symptoms and signs that can be highly variable and nonspecific, leading to frequent misdiagnosis. Both Dubin-Johnson syndrome (choice C) and Rotor syndrome manifest as conjugated hyperbilirubinemia. Both reflect a defect in biliary excretion and are relatively benign because the conjugated bilirubin is much less toxic than the unconjugated molecule. Gilbert syndrome (choice D) is caused by an abnormality in the TATA-box of the UGT promoter so expression of functional UGT is reduced, thus the reduced severity of the disorder.

QUESTION 277
Acromegaly is characterized by protruding jaw, enlargement of the nose, hands, feet, and skull, and a thickening of the skin. This disorder is the result of excessive production of which of the following hormones?

A. corticotropin-releasing hormone
B. GnRH
C. growth hormone
D. insulin-like growth factor-II (IGF-II)
E. thyroid-stimulating hormone

Correct Answer: C
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Acromegaly results when there is an excess production of growth hormone after epiphysial closure and cessation of long bone growth. Excessive production of corticotropin-releasing hormone (choice A) would result in an increase in ACTH production, which would lead to enhanced glucocorticoid and mineralocorticoid production. Excessive production of GnRH (choice B) would lead to increased production of LH, FSH, and hCG, with consequent effects on the female reproductive system. Excessive production of IGF-II (choice D) could lead to abnormal neonatal development since it is expressed only during this period. Excessive production of thyroid-stimulating hormone (choice E) would lead to increased release of the thyroid hormones, leading to multisystemic involvement such as rapid heart rate, nervousness, inability to sleep, weight loss, excessive sweating, and sensitivity to heat.

QUESTION 278
Under conditions of anaerobic glycolysis, the NAD+ required by glyceraldehyde-3-phosphate dehydrogenase is supplied by a reaction catalyzed by which of the following enzymes?

A. glycerol-3-phosphate dehydrogenase
B. alpha-ketoglutarate dehydrogenase

C. lactate dehydrogenase
D. malate dehydrogenase
E. PDH

Correct Answer: C
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
When glycolysis (a cytoplasmic pathway) is proceeding under anaerobic conditions, the electrons transferred to NAD+ (generating NADH) during the G3PDH-catalyzed step cannot be transferred to mitochondrial NADH nor FADH2, which would regenerate cytoplasmic NAD levels. This would lead to a deficiency in the NAD required by G3PDH and an eventual cessation of glycolysis. Therefore, under anaerobic conditions, tissues such as skeletal muscle reduce pyruvate (the end product of anaerobic glycolysis) to lactate catalyzed by LDH. This reaction requires electrons to be donated from NADH and thereby regenerate NAD, which can be used by G3PDH. If PDH (choice E) were to use any NAD in the oxidation of pyruvate to acetyl-CoA, there would be reduced levels available for G3PDH and glycolysis would cease, hence pyruvate is reduced by LDH. The citric acid cycle enzymes, alphaketoglutarate dehydrogenase (choice B) and malate dehydrogenase (choice D), in addition to being in the mitochondria, reduce NAD+ to NADH, therefore, neither would be able to supply glycolysis with NAD+. Although there is a cytoplasmic malate dehydrogenase and glycerol-3- phosphate dehydrogenase (choice A) is cytoplasmic, these enzymes are involved in the transfer of cytoplasmic electrons from NADH into the mitochondria, a process that is restricted by the lack of

O_2

during anaerobic metabolism.

QUESTION 279
The level of iron in the body must be tightly regulated due to the severe toxicity associated with elevated levels in the circulation and within cells. Which of the following proteins is primarily responsible for iron homeostasis?

A. ceruloplasmin
B. ferritin
C. haptoglobin
D. metallothionein
E. transferrin

Correct Answer: E
Section: Biochemistry
Explanation

Explanation/Reference:

Explanation:
Transferrin is a glycoprotein synthesized in the liver having a central role in the body's metabolism of iron. Each mole of transferring can transport 2 moles of in the circulation to sites where iron is

Fe^{3+}

required. Free iron is toxic, but when associated with transferrin this toxicity is greatly diminished. When bound to transferrin, iron can be directed to cells where it is needed. Many cells have transferrin receptors and on binding, the transferrin-receptor complex is internalized. The acidic pH of the lysosome causes the iron to dissociate from transferrin. Iron-free transferrin is then recycled to the cell surface along with its receptor, where it then reenters the circulation. Ceruloplasmin (choice A) is the major copper carrier of the body and is also synthesized in the liver. Ferritin (choice B) is an intracellular iron-binding protein. It does not play a role in iron metabolism or transport, and its function is to prevent ionized iron ( ) from reaching toxic levels within cells. Haptoglobin (choice

Fe^{2+}

C) is a plasma glycoprotein that binds extracorpuscular (free) hemoglobin. This function of haptoglobin is to prevent free hemoglobin from being lost through the kidneys, since the haptoglobin- hemoglobin complex is too large to pass through the glomerulus. Metallothioneins (choice D) are found in many cells and can bind copper, zinc, cadmium, and mercury.

QUESTION 280
Alaboratory analysis of isolated mitochondria demonstrates that oxygen consumption is normal when succinate is added, but extremely low when pyruvate and malate are used. The mitchondria are subsequently shown to have normal cytochromes, but reduced iron content. The reduced pyruvate/malate oxidation is due to a defect in which of the following respiratory components?

A. cytochrome c
B. cytochrome oxidase
C. NADH-coenzyme Q reductase
D. succinate dehydrogenase
E. ubiquinone

Correct Answer: C
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
During the process of oxidative phosphorylation, electrons from reduced electron carriers enter the pathway at either complex I or complex II. The reduced electron carrier, derived from the oxidation of pyruvate and malate (NADH), enters the oxidative phosphorylation machinery at complex I, NADH- coenzyme Q reductase (also identified as NADH-ubiquinone oxidoreductase). Whereas, the reduced electron carrier generated during the oxidation of succinate (FAD) enters the oxidative

H_2

phosphorylation machinery at complex II. Thus, a defect in the activity of complex I would inhibit oxygen consumption in the presence of pyruvate or malate but not succinate. The pathway of electron flow through the electron transport assembly has been determined through the uses of compounds termed antimetabolites. Some of these agents are inhibitors of electron transport at specific sites in the electron transport assembly, while others stimulate electron transport by discharging the proton gradient (uncouplers). An important example of an uncoupler is 2,4-dinitrophenol (DNP). Uncoupling agents, such as DNP, act as lipophilic weak acids, associating with protons on the exterior of mitochondria, passing through the membrane with the bound proton, and dissociating the proton on the interior of the mitochondrion. These agents cause maximum respiratory rates but the electron transport generates no ATP, since the translocated protons do not return to the interior through ATP synthase. Cytochrome c (choice A) receives electrons from complex III, cytochrome oxidase (choice B) receives electrons from cytochrome c, succinate dehydrogenase (choice D) is a component of complex II, and ubiquinone (choice E) receives electrons from both complex I and II, therefore, a defect in any of these proteins would not account for the observed phenomena.

QUESTION 281
The phosphorylase kinase-associated regulatory protein identified by the letter A in below figure is a calcium-binding protein. Which of the following proteins represents this regulatory subunit?

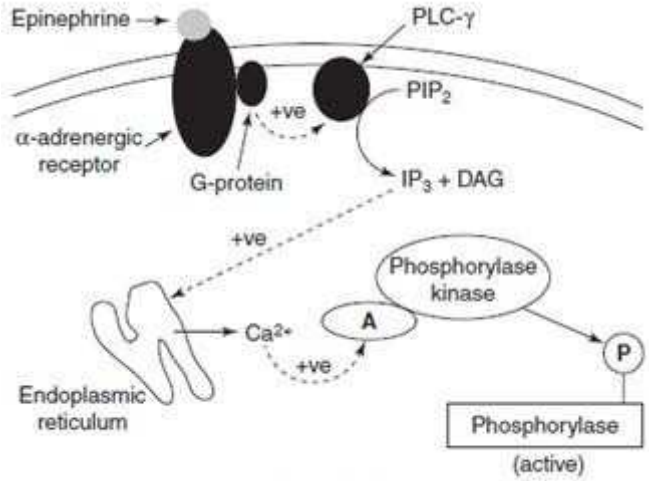


FIG. 3-4

A. calmodulin
B. fructose-2,6-bisphosphate
C. glycogen synthase kinase-3
D. phosphoprotein phosphatase
E. phosphoprotein phosphatase inhibitor-1

Correct Answer: A
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Phosphorylase kinase (also referred to as phosphorylase/synthase kinase, because it can phosphorylate both glycogen phosphorylase and glycogen synthase) contains calmodulin as a subunit. The presence of calmodulin allows phosphorylase kinase to be activated in the absence of a cAMP-mediated phosphorylation cascade. This is important when muscle is stimulated by epinephrine binding to alpha- adrenergic receptors (this function is diagrammed in below figure) or by acetylcholine release at the neuromuscular junction. Each of these events leads to increases in intracellular C . Each of the

a^{2+}

other proteins (choices B, C, D, and E) are independent activities not associated with phosphorylase kinase.

QUESTION 282
Mosaicism refers to a condition in which an individual has two or more genetically distinct cell types, derived from a single zygote, but that differ because of mutation or chromosomal aberration. Mosaicism occurs with a frequency of approximately 30% in females who are phenotypically normal but harbor gonadal dysgenesis, sexual immaturity, and infertility. These affected females also are short in stature, have webbing of the neck, and swelling of the hands and feet, as well as cardivascular and renal abnormalities. These symptoms are associated with which of the following diseases?

A. achondroplasia
B. Duchenne muscular dystrophy
C. fragile X syndrome
D. Kleinfelter syndrome
E. Turner syndrome

Correct Answer: E
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Turner syndrome is characterized by phenotypically normal females who are sexually immature and have gonadal dysgenesis and a host of somatic abnormalities. These symptoms arise due to chromosomal abnormalities in one of the X chromosome as well as due to monosomy for the X chromosome. Only around 5% of monosomy X fetuses survive to birth. Some 15% of Turner syndrome females are mosaic for the karyotype 45,X:46,XX and another 15% are mosaic for a 45,X cell line plus a 46,X, abnormal X cell line or a 47,XXX cell line. Achondroplasia (choice A) is the single most common form of dwarfism, which results from two specific defects in the gene encoding fibroblast growth factor receptor 3 (FGFR3). Symptoms of achondroplasia include rhizomelic short stature, midface hypoplasia, short ribs, and trident hand. DMD (choice B) is an X-linked condition whose symptoms occur in affected males in early childhood and only very rarely affects females.

DMD is caused by defects in the dystrophin protein, which is involved in the contractile apparatus of muscle cells. Fragile X syndrome (choice C) is the most common form of inherited mental retardation. The symptoms result from the loss of a portion of the X chromosome due to a site of fragility caused by the amplification of a trinucleotide repeat sequence in the FMR1 gene. Symptoms of fragile X are most severe in males (affected females have much milder symptoms) and include severe mental retardation and facial abnormalities such as prominent jaw, forehead, and ears. Kleinfelter syndrome (choice D) is associated with males harboring two or more X chromosomes (e.g., 47,XXY). Symptoms appear in puberty and affected individuals have a greater than expected frequency of social pathology. Although significant mental retardation is not associated with most Kleinfelter patients, the more X chromosomes and individual harbors the higher likelihood of mental retardation.

QUESTION 283
Achild born and raised in Chicago planned to spend the summer on a relative's fruit farm and help with the harvest. The summer passed uneventfully, but several days after the harvest began the child became jaundiced and very sick. On admission to the hospital the following clinical findings were recorded: in addition to the expected hyperbilirubinemia, the patient was hypoglycemic, had a markedly elevated rise in blood fructose concentration, and was hyperlactic acidemic. Further history taking revealed that during the harvest it was customary for the family to indulge in fruit-filled meals and to snack freely on fruit while carrying out the harvest. The following conclusions were reached. The elevated blood fructose was due to which of the following?

A. an allergic reaction to constituents in the fruit diet
B. defective hepatic fructokinase
C. defective hepatic glucokinase
D. defective hepatic fructose-1-phosphate aldolase (aldolase B)
E. defective hepatic fructose-1,6-bisphosphate aldolase (aldolase A)

Correct Answer: D
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Patients with hereditary fructose intolerance have defective function in hepatic fructose-1-phosphate aldolase (also called aldolase B). This enzyme hydrolyzes fructose-1-phosphate to glyceraldehyde and dihydroxyacetone phosphate. The reaction is the second in the hepatic pathway of fructose metabolism, the initial one being the phosphorylation of fructose at the 1 position by fructokinase (choice B). When fructose is high in the diet (as in the consumption of large quantities of fruit) the capability to divert the fructose into the glycolytic pathway is severely impaired. Fructose becomes trapped in the liver as fructose-1-phosphate. Due to the lack of aldolase B, the capacity to phosphorylate fructose becomes limiting due to feedback inhibition of fructokinase, resulting in an elevation in serum fructose levels. Hepatic glucokinase (choice C) and aldolase A (choice E) are not involved in the metabolism of fructose. An allergic reaction (choice A) would not manifest with elevated serum fructose, hyperbilirubinemia, or hyperlacticacidemia.

QUESTION 284
The incretins are hormones that are released in response to the consumption of food. Which of the following represents one of the major effects of incretin release from intestinal epithelial cells?

A. activation of gastric emptying ensuring release of ingested food

B. enhancement in adipocyte triacylglycerol synthesis
C. enhancement of insulin secretion from the pancreas
D. repression of pancreatic cell proliferation
E. stimulation of gastric acid secretion to aid in digestion

Correct Answer: C
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
The incretins are molecules associated with food intake-stimulation of insulin secretion from the pancreas. Two of the many GI hormones have significant effects on insulin secretion and glucose regulation. These hormones are GLP-1 and glucose-dependent insulinotropic peptide (GIP). Both of these gut hormones represent the incretins. In contrast to activation of gastric emptying (choice A) and repression of pancreatic cell proliferation (choice D), GLP-1 inhibits gastric emptying and promotes a sense of satiety, induces proliferation, and represses apoptosis of pancreatic beta-cells. The incretins do not enhance adipose triacylglycerol synthesis (choice B). Repression of gastric acid secretion, not sitmulation (choice E) is one of the additional functions of GIP.

QUESTION 285
PDH is a complex multisubunit enzyme. Which of the following exerts a positive influence on the activity of PDH?

A. acetyl-CoA
B. ATP
C. dephosphorylation
D. NADH
E. phosphorylation

Correct Answer: C
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Regulation of the PDH complex is effected by both allosteric means and by phosphorylation (see below figure). Allosteric effectors of the enzyme complex are of both positive and negative type. The complex is phosphorylated by a specific kinase identified as PDH kinase and phosphate is removed by PDH phosphatase. When in the unphosphorylated state the complex is much more active, therefore the activity of PDH phosphatase is important for maintaining the PDH complex in the active state. Acetyl- CoA (choice A) and NADH (choice D) are both allosteric inhibitors of the nonphosphorylated form of the PDH complex and also serves to activate PDH kinase leading to phosphorylated and inhibited PDH. Like acetyl- CoA and NADH, ATP (choice B) allosterically activates the PDH kinase leading to phosphorylated and inhbited PDH. Phosphorylation (choice E) inhibits the activity of the PDH complex.

QUESTION 286
Vitamin K serves as a coenzyme in reactions that result in the modified activity of several enzymes of the blood coagulation cascade. Which of the following amino acid modifications requires the activity of vitamin K?

A. aspartate to beta-carboxyaspartate
B. glutamate to gamma-carboxyglutamate
C. lysine to hydroxylysine
D. lysine to beta-methyllysine
E. proline to hydroxyproline

Correct Answer: B
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
factors II, VII, IX, X, and protein C) bind calcium and are thus activated following cleavage of their zymogen forms. The ability of these proteins to bind calcium requires posttranslationally modified glutamate residues. The modification is a gamma-carboxylation yielding gamma-carboxyglutamate (gla) residue. The carboxylation reaction has an absolute requirement for vitamin K as a cofactor. None of the other amino acid modifications (choices A, C, D, and E) require vitamin K as a cofactor. Hydroxylation of proline (choice E) and lysine (choice C) is carried out by enzymes that require vitamin C as a cofactor.

QUESTION 287
Steroid hormones interact with specific receptors within target cells. The steroid-receptor complexes then regulate the rate of which of the following intracellular processes?

A. posttranscriptional processing of specific mRNAs
B. posttranslational processing of specific proteins
C. replication of DNA
D. transcription of specific genes
E. translation of specific mRNAs

Correct Answer: D
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Steroid hormones are lipophilic and hence freely penetrate the plasma membrane of all cells. Within target cells, steroid hormones interact with specific receptors. These receptor proteins are composed of two domains: a hormone-binding domain and a DNA-binding domain. Following hormone-receptor, interaction the

complex is activated and enters the nucleus. The DNA-binding domain of the receptor interacts with specific nucleotide sequences termed hormone response elements (HREs). The binding of steroid-receptor complexes to HREs results in an altered rate of transcription of the associated gene(s). The effects of steroid-receptor complexes on specific target genes can be either stimulatory or inhibitory with respect to the rate of transcription. Complexes of steroid with receptor have no direct effect on posttranscriptional processing of RNA (choice A), posttranslational events (choice B), DNA replication (choice C), or translation (choice E).

QUESTION 288
Resistance to Type I diabetes has been shown to be associated with a specific polymorphic allele.
Which of the following loci represents this allele?

A. a VNTR in the 5' region of the insulin gene
B. glutamic acid decarboxylase (GAD)
C. HLA-B27
D. HLA-DQ
E. HLA-DR3

Correct Answer: D
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Class I and class II genes of the major histocompatibility locus (MHC), which comprise the HLA genes, are highly polymorphic and express hundreds of different alleles in humans. Many of these polymorphic loci are associated, either positively or negatively, with autoimmune-related disorders. Inheritance of the class II HLA-DQ allele has been highly correlated to resistance to development of Type I diabetes. Conversely, the DR3 allele (choice E) is positively correlated with development of Type I diabetes. Autoantibodies to GAD (choice B) are found in over 80% of patients with Type I diabetes. Different VNTR structure present in the promoter region of the insulin gene (choice A) has been shown to indicate susceptibility to Type I diabetes. The HLA-B27 allele (choice C) is correlated with ankylosing spondylitis.

QUESTION 289
The inability to rapidly synthesize DNA during the process of erythrocyte maturation leads to abnormally enlarged erythrocytes. This disorder is referred to as macrocytic anemia and is caused by a deficiency in which of the following vitamins?

A. ascorbate
B. biotin
C. folate
D. niacin
E. thiamine

Correct Answer: C

Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Folic acid is the vitamin component of tetrahydrofolate, THF. Folic acid is reduced within cells (principally the liver where it is stored) to THF through the action of dihydrofolate reductase (DHFR), an NADPH-requiring enzyme. The function of THF derivatives is to carry and transfer various forms of one carbon units during biosynthetic reactions. One of the more important roles for THF is in the conversion of dUMP to dTMP catalyzed by thymidylate synthase, with the methyl group being donated by , -methylene-THF. Folate deficiency results in complications nearly identical to those

N^5

described for vitamin deficiency. The most pronounced effect of folate deficiency on cellular

B_{12}

processes is on DNA synthesis due to an impairment in dTMP synthesis. This leads to cell-cycle arrest in S-phase of rapidly proliferating cells, in particular hematopoietic cells. Deficiencies in ascorbate, vitamin C (choice A), leads to defects in collagen processing and the disorder is identified as scurvy. Deficiencies in biotin (choice B) are extremely rare but would manifest as hypoglycemia following fasting due to the role of biotin in gluconeogenesis at the pyruvate carboxylase step. Deficiencies of niacin, , (choice D) are characterized by the "3 Ds": depression, dermatitis, and diarrhea and are

B_3

associated with the condition known as pellagra. Deficiencies in thiamin (choice E) cause constipation, appetite suppression, nausea as well as mental depression, peripheral neuropathy, and fatigue. Chronic thiamin deficiency leads to more severe neurologic symptoms including ataxia, mental confusion, and loss of eye coordination. The severe thiamin deficiency disease known as beriberi is the result of a diet that is carbohydrate rich and thiamin deficient. An additional thiamin deficiency related disease is known as Wernicke-Korsakoff syndrome. This disease is most commonly found in chronic alcoholics due to their poor dietetic lifestyles.

QUESTION 290
A 12-year-old boy has suffered from chronic sinopulmonary disease including persistent infection of the airway with Pseudomonas aeruginosa. He has constant and chronic sputum production as a result of the airway infection. Additionally, he suffers from gastrointestinal (GI) and nutritional abnormalities that include biliary cirrhosis, meconium ileus, and pancreatic insufficency. The symptoms are classical for which of the following disorders?

A. congenital adrenal hyperplasia
B. CF
C. Renal Fanconi syndrome
D. sickle cell anemia
E. Tay-Sachs disease

Correct Answer: B
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
CF affects a number of organ systems including the lung and upper respiratory tract, liver, pancreas, and sweat glands. Classical symptoms of individuals with CF are chronic airway infection with P. aeruginosa and Staphylococcus aureus. CF results from deficiencies in the gene encoding the CFTR. The protein encoded by this gene is a member of the ATPbinding cassette (ABC) transporter family of proteins. Although multiple organ systems are affected by defects in the CFTR gene, morbidity and mortality results primarily from impairment of the pulmonary defense system. Congenital adrenal hyperplasia, CAH (chioice A) constitutes a group of diseases whose common features result from defects in the pathway leading to cortisol synthesis. The most frequent defects occur in the 21- hydroxylase gene (CYP21) that catalyzes the conversion of progesterone to 11-deoxycorticosterone and 17-hydroxyprogesterone to 11-deoxycortisol. Deficiency in CYP21 leads to loss of cortisol and aldosterone secretion and maximal secretion of the adrenal androgens. The effect on female development is masculinization of the external genitalia. Renal Fanconi syndrome (choice C) is acquired either through exposure to toxic agents or due to various inborn errors in metabolism that lead to generalized dysfunction of the proximal renal tubules. Affected individuals exhibit a characteristic vitamin Ddeficient metabolic bone disease, polyuria, polydipsia, hypokalemia, and acidosis. Sickle cell anemia (choice D) results from a mutation in the beta-globin gene and is characterized by lifelong hemolytic anemia, an increased propensity to infection, and complications resulting from repeated vascular occlusions that result during cycling crises. Tay-Sachs disease (choice E) is a fatal disease of early childhood resulting from a deficiency in the hexosaminidase A enzyme. Hexosaminidase A is required for the catabolism of complex sphingolipids (G gangliosides) and defects in the enzyme

M_2

lead to severe neurologic impairment.

QUESTION 291
Exhbit:

A. arachidonic acid
B. leukotriene B_4
C. platelet-activating factor (PAF)
D. prostaglandin E_2
E. thromboxane A_2 (TXA_2)

Please refer to the exhibit.
Hypersensitive individuals have IgE to specific antigens (e.g., pollen, bee venom) on the surface of their leukocytes (monocytes, macrophages, basophils, eosinophils). When these individuals are challenged with antigen, the antigen-IgE complexes induce synthesis and release of which of the following physiologically

potent lipids?

A. A
B. B
C. C
D. D
E. E

Correct Answer: C
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
PAF is a unique complex lipid of the plasmalogen family. PAF functions in hypersensitivity, acute inflammatory reactions, and anaphylactic shock by increased vasopermeability, vasodilation, and bronchoconstriction. Excess production of PAF production may be involved in the morbidity associated with toxic shock syndrome and strokes. Arachidonic acid (choice A) is the precursor lipid for the eicosanoids, which includes the prostaglandins, thromboxanes, and leukotrienes. Leukotriene (choice B) induces leukocyte chemotaxis and aggregation. Prostaglandin (choice D) increases

B_4

vasodilation, enhances effects of bradykinin and histamine, induces uterine contractions and platelet aggregation. Thromboxane (choice E) induces platelet aggregation and vasoconstriction.

A_2

QUESTION 292
Acetyl-CoA enhances the rate of gluconeogenesis by acting as an allosteric activator of which of the following enzymes?

A. ACC
B. PEP-carboxykinase
C. pyruvate carboxylase
D. PDH
E. pyruvate kinase

Correct Answer: C
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
The major substrates of gluconeogenesis are pyruvate and lactate. During gluconeogenesis lactate is oxidized to pyruvate. For pyruvate to be converted back to glucose, it must first be carboxylated to oxaloacetate, since a reversal of the PK reaction of glycolysis cannot occur to convert the pyruvate to phosphoenolpyruvate. The carboxylation of pyruvate is catalyzed by the mitochondrial enzyme pyruvate carboxylase. The activity of pyruvate carboxylase is absolutely dependent on the presence of acetyl-CoA, which allosterically activates the enzyme. Of the enzymes listed, only pyruvate carboxylase and PEPCK (choice B) are involved in gluconeogenesis. ACC (choice A) is involved in fatty acid synthesis and is not regulated by acetyl-CoA. PDH (choice D) is the entry point for pyruvate into the TCA cycle. It is also inhibited by acetyl- CoAvia the acetyl-CoA-mediated activation of PDH kinase, an enzyme that phosphorylatesand inactivates PDH. PK (choice E) is a glycolytic enzyme and is inhibited by acetyl-CoA, not activated by it.

QUESTION 293
You are studying the effects of a compound on the respiratory activity of isolated mitochondria. Your experiments demonstrate that oxygen consumption is normal when pyruvate and malate are added. Oxygen consumption is also seen to be normal when succinate is added. However, you find that the production of ATP is severely impaired in the presence of pyruvate/malate or succinate when the compound is added to the reaction. These results most closely resemble the effects that would be seen by the addition of which of the following inhibitors of oxidative phosphorylation?

A. antimycin A
B. azide
C. dinitrophenol
D. oligomycin
E. rotenone

Correct Answer: C
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
The normal flow of electrons, through the proteins of the oxidative phosphorylation machinery, is coupled with the establishment of a proton gradient across the inner mitochondrial membrane. The establishment of this pH gradient is the chemiosmotic potential that is coupled with the production of ATP. If the process of proton movement is uncoupled from the normal pathway through the ATP synthase complex, oxygen can be consumed but no ATP will be synthesized. This is the effect of uncoupling agents such as DNP, which act to discharge the proton gradient. Antimycin A (choice A) is an antibiotic that functions by inhibiting cytochrome b of complex III. Azide (choice B) inhibits cytochrome oxidase of complex IV. Oligomycin (choice D), a streptomyces antibiotic, inhibits ATP synthase. Rotenone (choice E) inhibits complex I.

QUESTION 294
An observation that has been made over the past several decades is that certain dominantly inherited disorders exhibit earlier age of onset along with increasing severity in successive generations. This phenomenon is referred to as anticipation. Amost striking example of this genetic trait is characterized by muscle wasting beginning with the face, neck, and hands gradually becoming generalized and by the inability of muscles to relax after contraction. These symptoms and the phenomenon of anticipation are associated with which of the following diseases?

A. becker muscular dystrophy (BMD)
B. DMD
C. Marfan syndrome
D. myotonic dystrophy
E. osteogenesis imperfecta

Correct Answer: D
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Myotonic dystrophy is the most common muscular dystrophy affecting adults. Apart from the clinical manifestations of the disease described in the question, myotonic dystrophy affects cardiac and smooth muscles, is associated with immune disorder, minor mental retardation, and cataracts. Myotonic dystrophy results from defects in the myotonin gene. These defects are associated with the expansion of a trinucleotide repeat sequence in the 3'- untranslated region of the gene. BMD (choice A) and DMD (choice B) both result from mutations in the DMD gene, but the symptoms of BMD are milder than those of DMD. Transmission of these two diseases is X-linked. Marfan syndrome (choice C) and osteogenesis imperfect are disorders of connective tissue. Marfan syndrome results from defects in the fibrillin gene and osteogenesis imperfecta from defects in collagen. None of the other four diseases exhibit the inheritance phenomenon of anticipation.

QUESTION 295
The bacterial lac operon is controlled by both glucose and lactose levels. Which of the following conditions would result in the greatest level of transcription from the lac operon?

A. both glucose and lactose present
B. glucose present but no lactose
C. lactose present but no glucose
D. no glucose or lactose present

Correct Answer: C
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
The lac operon in bacteria is a group of three coordinately regulated genes whose functions are to allow the bacterium to survive when glucose is low or absent as an energy source. The major nonglucose source of energy is from lactose, a disaccharide of glucose and galactose. The control of expression from the lac operon by glucose is exerted through the level of cAMP, whereas, control by lactose is exerted through induced inhibition of the repressor of the operon. When glucose levels are plentiful, the level of cAMP is low. The role of cAMP in the regulation of the lac operon is to bind to the catabolite activator protein (CAP), which is a DNA-

binding factor that stimulates the activity of RNA polymerase. As glucose levels drop, cAMP levels rise with a concomitant increase in CAP-mediated activation of polymerase. In the presence of lactose, the lac operon repressor protein is prevented from binding to the operator region of the operon resulting in an increase in the rate of transcription. Therefore, maximal activity would be seen with no glucose in the presence of lactose. With both glucose and lactose present (choice A), the level of cAMP would be low so there would be no activation of polymerase via CAP, but some level of transcription would occur due to the lactosemediated inhibition of the repressor activity. With glucose and no lactose (choice B) the lac operon would be maximally repressed since CAP would be inactive and repressor would be uninhibited. With no glucose or lactose (choice D), the level of cAMP would be high so activation of CAP would be evident leading to transcription, but due to the presence of the repressor the rate of transcription would not be maximal.

QUESTION 296
The term "genomic imprinting" refers to the phenomenon of gene expression dependence on the mode of inheritence. A typical example of this phenomenon is the control of the expression of the growth factor IGF-II. Genomic imprinting, termed "epigenesis," is defined by which of the following?

A. Gene expression results from regulated levels of DNA methylation.
B. Gene expression that is restricted to a specific cell lineage.
C. Gene regulation is exerted by sex-type specifc factors.
D. Genotype differences are not reflected by phenotype differences.
E. Phenotype differences are independent of genotype variation.

Correct Answer: E
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Epigenesis refers to the phenomenon where phenotypic differences are present in the same species, but this difference is not due to differences in the genotype of the organism. None of the other examples (choices AD) define epigenesis.

QUESTION 297
The process of RNA editing leads to sequence changes that are not reflective of the genetic information contained within the gene for an edited RNA. RNA editing occurs through the action of specific nucleotide deaminases that change either adenine to inosine or cytidine to uridine. These nucleotide changes can affect the coding or splicing capacity of the RNA. Which of the following proteins is an important example of the result of RNA editing?

A. apo B48
B. calcitonin gene-related peptide
C. ferritin
D. glutamate dehydrogenase
E. tissue factor (factor III)

Correct Answer: A

Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
RNA editing in mammals involves the deamination of adenine A. to produce inosine (I) in pre- mRNAs. The process of Ato I editing is catalyzed by ADARs (ADAs acting on RNA). In some pre- mRNAs this alters splicing; in some it alters codon(s). RNA editing also occurs to convert C to U. A C to Uedit in the gene for apo B leads to tissue-specific generation of apo in intestines, whereas the

B_{48}

nonedited mRNA makes apo in liver. None of the other gene products (BE) result from RNA

B_{100}

editing, although the generation of the CGRP is the result of another posttranscriptional phenomenon:
alternative splicing and alternative polyadenylation site usage.

QUESTION 298
Carnitine, a zwitterionic compound derived from lysine, is involved in fatty acid metabolism and is required at which two points in the transport of fatty acids from the cytoplasm to the mitochondria (see below figure)?

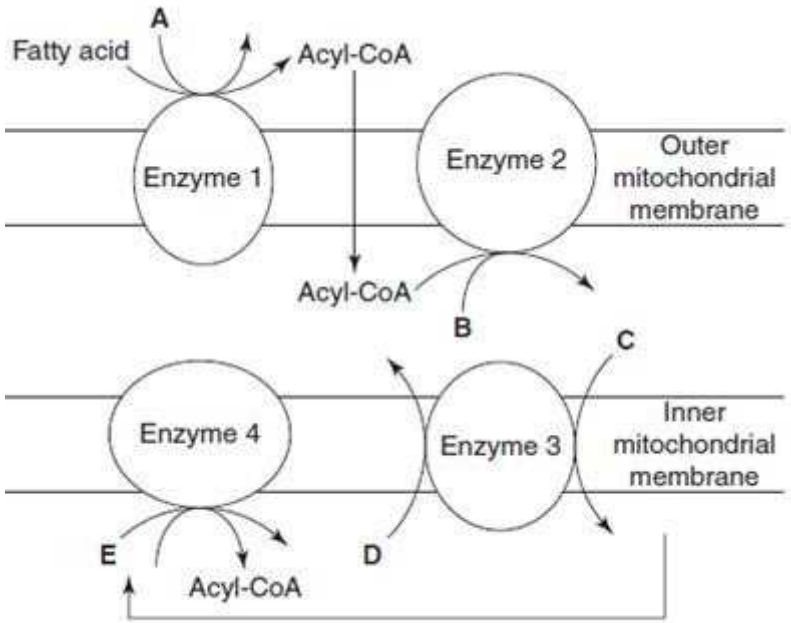


FIG. 3-5

A. A and E
B. A and C
C. B and C
D. B and D
E. E and D

Correct Answer: D
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Fatty acids are activated to the CoA derivatives at the outer mitochondrial membrane (catalyzed by enzyme 1 in below figure), but are oxidized inside the mitochondria. Long-chain fatty acyl-CoA molecules do not cross the mitochondrial membrane. A special transport system involving carnitine is used for movement of the activated fatty acids into the mitochondria. The fatty acyl moiety is transferred from the CoA to carnitine in a reaction catalyzed by carnitine acyltransferase I (enzyme 2 in below figure). Acyl carnitine thus formed is shuttled across the inner mitochondrial membrane (via enzyme 3 in below figure), where the fatty acyl group is transferred back to a CoA molecule within the mitochondrial matrix. The latter reaction is catalyzed by carnitine acyltransferase II (enzyme 4 in below

figure). Medium-chain fatty acyl-CoAs can cross the mitochondrial membrane and do not require the carnitine transport system for entry into the mitochondria. The compound(s) at point Aare ATP and CoA, point B is carnitine, point C is acylcarnitine, point D is carnitine, and E is acylcarnitine. Therefore, the requirements for carnitine occur on either side of the inner mitochondrial membrane at points B and D, which occur during the translocation process. All other combinations (choices A, B, C, and E) have a compound or compounds other than or in addition to carnitine.

QUESTION 299
When the body becomes acidotic, the liver and the kidneys play central roles in reactions designed to reduce the proton level (i.e., increase the pH) of the circulation. Which of the following constitutes the hepatic reaction occuring during periods of acidosis?

A. ammonia incorporation into glutamateforming glutamine
B. ammonia incorporation into alphaketoglutarate- forming glutamate
C. glutamine conversion to glutamatereleasing ammonia
D. glutamine conversion to alphaketoglutarate- releasing ammonia
E. increased production of urea to dispose of ammonia

Correct Answer: A
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Major reactions, that involve the regulation of plasma pH as well as the level of circulating ammonia, involve the heptatic and renal enzymes GDH, glutamine synthase (GS), and glutaminase. The liver compartmentalizes GS and glutaminase in order to control the flow of ammonia into glutamine or urea. Under acidotic conditions the liver diverts ammonia to glutamine via the GS reaction. The glutamine then enters the circulation. In fact, glutamine is the major amino acid of the circulation and its role is to ferry ammonia to and from various tissues. In the kidneys, glutamine is hydrolyzed by glutaminase (yielding glutamate) releasing the ammonia to the urine. There the ammonia ionizes to ammonium ion, $N +$, which reduces the circulating concentration of hydrogen ion resulting in an increase in the pH.

H_4

Additionally, the glutamate can be converted to alphaketoglutarate yielding another mole of ammonia, which is ionized by hydrogen ions further increasing the pH. Incorporation of mmonia into alpha- ketoglutarate (choice B) would deplete the ammonia ionization reaction and lead to further acidification. Glutamine conversion to glutamate (choice C) will occur in the kidneys but not in the liver under acidotic conditions. Glutamine is not directly converted to alpha-ketoglutarate (choice D); a two-step process is required and would take place in the kidneys not in the liver under acidotic conditions as in choice C. Conversion of ammonia into urea (choice E) is the process of ridding the body of waste nitrogen, but it is not a means to regulate the pH of bodily fluids.

QUESTION 300
The occurrence of Type II diabetes (NIDDM) in adolescent females can lead to the development of polycystic ovarian syndrome (PCOS). PCOS is the result of follicular atresis and ovulatory dysfunction brought about by a hyperandrogenic microenvironment in the ovary. Which of the following statements reflects the underlying cause of the hyperandrogenic state in females with NIDDM?

A. Hyperinsulinemia, associated with NIDDM, reduces the level of sex hormone-binding globulin leading to increased free testosterone.
B. NIDDM in adolescents is primarily the result of obesity and the associated disruption in fatty acid metabolism negatively affects adrenal estrogen production.
C. The increased level of circulating lipid in NIDDM patients competes for steroid binding to sex hormone-binding globulin, resulting in a reduced transport of estrogen within the ovary.
D. The persistent hyperglycemia associated with NIDDM causes increased levels of glycosylated hemoglobin, which interferes with the need for increased ovarian vascularization at puberty.

Correct Answer: A
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Adolescent females with Type II diabetes have a high occurrence of PCOS, which is brought on by the hyperinsulinemia associated with Type II diabetes. Insulin effects on the ovary drive conversion of progesterone to testosterone and a reduction in serum hormonebinding globulin (SHBG). Taken together, the effects of hyperinsulinemia lead to a hyperandrogenic state in the ovary resulting in follicular atresis and ovulatory dysfunction. None of the other options (choices BD) are associated effects caused by Type II diabetes leading to PCOS.

QUESTION 301
A 15-year-old boy has been diagnosed with retinitis pigmentosa, peripheral polyneuropathy, and cerebellar ataxia. Analysis of his cerebrospinal fluid indicated a high protein content but no elevation of cell number. A telling clinical finding was a high level of serum phytanic acid. These findings are indicative of which of the following disorders?

A. carnitine palmitoyltransferase I deficiency
B. fragile X syndrome
C. MCAD deficiency
D. Refsum disease
E. rhizomelic chondrodysplasia punctata

Correct Answer: D
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Refsum disease is the result of defects in the oxidation of phytanic acid, a lipid requiring an alpha- oxidation pathway. As a consequence, phytanic acid accumulates in the blood and tissues. The hallmark symptoms of the disease are retinitis pigmentosa, cerebellar ataxia, chronic polyneuropathy, and an elevation in protein in the cerebrospinal fluid with no increase in cell count. Adeficiency in carnitine palmitoyltransferase I (choice A) primarily affects the liver and results in

reduced fatty acid oxidation and ketogenesis. Fragile X syndrome (choice B) is the most common form of heritable mental retardation worldwide. MCAD deficiency (choice C) is one of most frequently inherited defects in metabolism. Clinical crisis is characterized by an infant presenting with episodes of vomiting and lethargy, seizures, and coma associated with a period of fasting. On presentation, the infant may be comatose and blood glucose will be low with low to no ketones in urine. RCDP (choice E) is caused by a disorder in peroxisome biogenesis. Rhizomelia refers to striking shortening of the proximal limbs. Patients also have severely disturbed endochondral bone formation. In addition, RCDP patients have profound psychomotor retardation.

QUESTION 302
In analyzing a sample of double-stranded DNA, it has been determined that the molar ratio of adenosine is 20%. Given this information, what is the content of cytidine?

A. 10
B. 20
C. 30
D. 40
E. 60

Correct Answer: C
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
The molar ratio of adenosine in any molecule of double-stranded DNA will be equivalent to that of thymidine, since these two nucleotides hydrogen bond to form base pairs. Therefore, the total amount of the DNA accounted for in A-T base pairs would be 40%. Since guanosine and cytidine hydrogen bond to form base pairs, they too contribute an equivalent molar ratio in double-stranded DNA. In double-stranded DNA with 40% A-T composition, the molar ratio of cytidine would be half of the remaining 60% of the DNA, or 30%. No other molar ratio (choices A, B, D, and E) could account for the amount of cytidine in a double-stranded DNA with 20% adenosine.

QUESTION 303
Measurement of the rate of creatinine clearance is used as a key determinant of renal function. In which of the following tissues is creatinine generated?

A. adipose
B. kidney
C. liver
D. lung
E. skeletal muscle

Correct Answer: E
Section: Biochemistry

Explanation

Explanation/Reference:
Explanation:
In cardiac and skeletal muscle, high-energy phosphate is stored through the transfer of a phosphate from ATP to creatine-generating creatine phosphate. Creatine is synthesized in liver from guanidoacetate. Guanidoacetate is derived from the amino acid arginine in the kidneys (below figure). In muscle cells, creatinine is a nonenzymatic metabolite of creatine phosphate. When measured in the serum, levels of creatinine are remarkably constant from day to day and are proportional to muscle mass. In renal dysfunction, the clearance of creatinine will be impaired and its levels will therefore rise in the serum. Although creatine is synthesized in the liver (choice C) from guanidoacetate, which is produced in the kidneys (choice B), it is not used by these two tissues, nor by the lung (choice D) or adipose tissue (choice A). Once synthesized, creatine is transported to cardiac and skeletal muscle where it is phosphorylated and stored for future energy needs.

QUESTION 304
Numerous cancers are caused by a genetic phenomenon termed "loss of heterozygosity," LOH. This phenomenon led to the identification of genes termed tumor suppressors, because it is the loss of their function that leads to cancer. Which of the following has been shown to result from defects in a tumor suppressor gene as a consequence of LOH?

A. Creutzfeldt-Jakob disease (CJD)
B. Crouzon syndrome
C. HD
D. Li-Fraumeni syndrome (LFS)
E. Prader-Willi syndrome

Correct Answer: D
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
LFS is a rare inherited form of cancer that involves breast and colon carcinomas, softtissue sarcomas, osteosarcomas, brain tumors, leukemia, and adrenocortical carcinomas. These tumors develop at an early age in LFS patients. The tumor suppressor gene found responsible for LFS is p53. Mutant forms of p53 are found in approximately 50% of all tumors. The normal p53 protein functions as a transcription factor that can induce either cell-cycle arrest or apoptosis (programmed cell death) in response to DNA damage. CJD (choice A) encompasses three forms: infectious, sporadic, and inherited, with the vast majority of cases being sporadic. Clinical abnormalities of CJD are confined to the CNS and result from a pathogenic protein identified as prion protein (PrP). Crouzon syndrome (choice B) is haracterized by craniosynostosis (midface hypoplasia and ocular proptosis) and is the result of a mutation in one of the receptors for fibroblast growth factor (FGFR2). HD (choice C) is an autosomaldominant disorder resulting from expansion of the triplet CAG within the huntingtin gene. The exact function of the huntingtin protein is still unclear. Symptoms of HD include personality changes, memory loss, and involuntary leg and arm movements (chorea). The average age of onset is 37 years. PWS (choice E) is a relatively common cause of genetic obesity and mental retardation. Symptoms of severe hypotonia and poor suckling are evident at birth. PWS is caused by a deletion of a portion of the long arm of chromosome 15 [del(15q11q13)].

QUESTION 305
Following a relatively normal early developmental period, a 6-month-old boy becomes pale and lethargic and begins to show signs of deteriorating motor skills. The

infant has severe megaloblastic anemia; however, serum measurements of iron, folate, vitamins and demonstrate they are

B_{12}

within normal range. Urine samples were clear when fresh, but when left to stand for several hours showed an abundant white precipitate that was composed of fine needle-shaped crystals. Analysis of the crystals identified them as orotic acid. Significant improvement is observed in the infant following oral administration of a nucleoside. Which of the following is most likely the nucleoside used?

A. adenosine
B. cytidine
C. guanosine
D. thymidine
E. uridine

Correct Answer: E
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Hereditary orotic aciduria results from a defect in the de novo synthesis of pyrimidines. The defect is in the bifunctional enzyme that catalyzes the last two steps in the de novo pathway, conversion of orotic acid to OMP and OMP to UMP. Administration of uridine allows afflicted individuals to produce sufficient levels of cytidine nucleotides via the salvage pathways. Treatment with uridine leads to a return of normal blood hemoglobin levels, and bone marrow will become normoblastic. Treatment with cytidine (choice B) has some limited ability to ameliorate symptoms of the disease, but not to the extent of uridine administration. None of the other nucleosides (choices A, C, and D) can be salvaged into cytidine or uridine nucleotides, and are therefore of no clinical value in the treatment of hereditary orotic aciduria.

QUESTION 306
If the DNA strand shown below is used as a template for RNA polymerase, what would be the sequence of the resultant mRNA following transcription?
5'-CATTCCATAGCATGT-3'

A. 5'-ACAUGCUAUGGAAUG-3'
B. 5'-CAUUCCAUAGCAUGU-3'
C. 5'-GUAAGGUAUCGUACA-3'
D. 5'-UGUACGAUACCUUAC-3'

Correct Answer: A
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Transcription occurs in the 5'3' direction, and during this process RNA polymerase will move in the 3'5' direction relative to the template DNA strand. Therefore, the correct transcriptional product from the DNA template begins with its 5' ribonucleotide corresponding to the complementary deoxyribonucleotide of the 3' end of the template. None of the other RNA strands (choices B, C, D, and E) could be products generated from the template shown.

QUESTION 307
If the RNA synthesized in Question 398 were translated in a eukaryotic in vitro translation system, what would be the composition of the resultant peptide?

ACA	threonine	(T)	CAU	histidine	(H)
ACG	threonine	(T)	CUA	leucine	(L)
AUG	methionine	(M)	CGU	arginine	(R)
AAU	asparagine	(N)	CCU	proline	(P)
AGG	arginine	(R)	UGC	cysteine	C.
AUA	isoleucine	(I)	UGU	cysteine	C.
GGA	glycine	(G)	UAU	tyrosine	(Y)
GUA	valine	(V)	UAC	tyrosine	(Y)
GCA	alanine	A.	UCC	serine	(S)
UGG	tryptophan	(W)			

A. C-T-I-P-Y
B. H-S-I-A-C
C. M-L-W-N
D. T-C-Y-G-M
E. V-R-Y-R-T

Correct Answer: C
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Translation in a eukaryotic in vitro translation system would begin at an AUG codon residing near the 5'-end of the mRNA. Therefore, translation of the correct RNA product would begin two nucleotides from the 5' end at the first AUG codon. This would result in the translation of a protein of four amino acids. None of the other choices (A, B, D, and E) translate into a four-unit amino acid chain.

QUESTION 308
Which of the following statements most correctly reflects the effect of epinephrine stimulation of adipocytes?

A. enzyme-dependent addition of fatty acids to glycerol-3-phosphate
B. enzyme-dependent stepwise release of fatty acids from triglycerides
C. increased synthesis and activation of LPL
D. increased synthesis of HDL to transport fatty acids to peripheral tissues
E. release of glycerol-3-phosphate for gluconeogenesis in the liver

Correct Answer: B
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
When epinephrine stimulates adipocytes (by interaction with beta-adrenergic receptors), the immediate response is the activation of adenylate cyclase, which in turn leads to an increase in cAMP. Increased levels of cAMP lead to activation of PKA, which in adipocytes will phosphorylate and activate hormonesensitive lipase. When hormone-sensitive lipase is active, it removes fatty acids in a stepwise manner from stored triacylglycerides. The released fatty acids then enter the blood and are bound by albumin for transport to peripheral tissues including the liver. LPL (choice C) is present on the surfaces of vascular endothelial cells and is activated by apo CII present in VLDLs and chylomicrons. Epinephrine is a stimulus that leads to energy consumption and therefore would not lead to an increase in triacylglyceride synthesis (choice A). When triacylglyceride breakdown is activated in adipocytes, the glycerol backbone is released as free glycerol, not glycerol-3-phosphate (choice E) to the blood and delivered to the liver for gluconeogenesis. Fatty acids released from adipose tissue are transported in the blood bound to albumin, not within any lipoprotein particle (choice D).

QUESTION 309
Which of the following familial cancers results from a defect in the tumor suppressor gene, p53?

A. familial adenomatous polyposis coli (APC)
B. Li Fraumeni syndrome
C. neurofibromatosis type 1
D. retinoblastoma
E. Wilms tumor

Correct Answer: B
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:

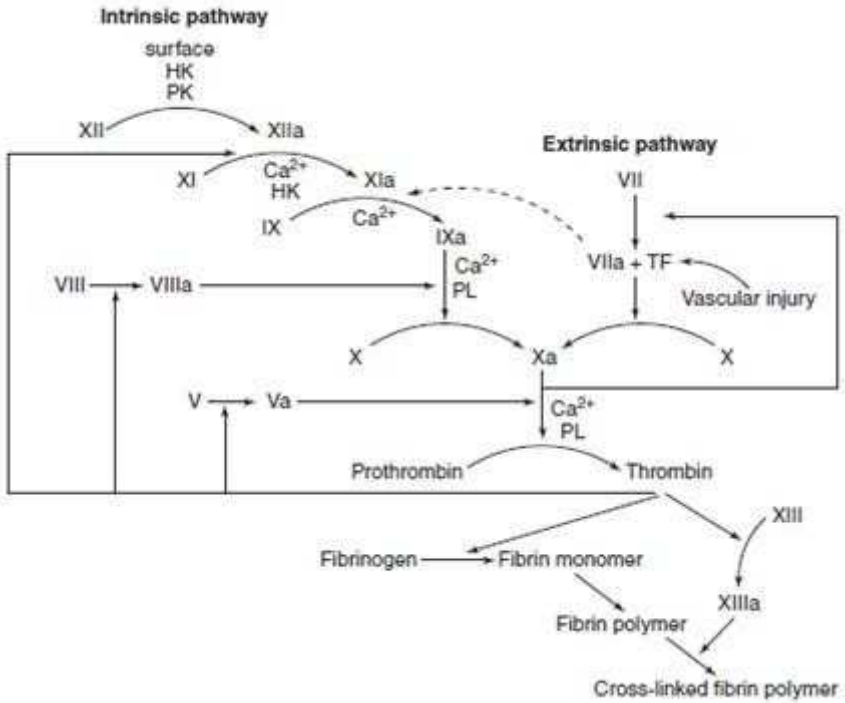
Numerous cancers are caused by the loss of function of tumor suppressor genes. LFS is a rare form of inherited cancer that involves breast and colon carcinomas, soft-tissue sarcomas, osteosarcomas, brain tumors, leukemia, and adrenocortical carcinomas. These tumors develop at an early age in LFS patients. The tumor suppressor gene found responsible for LFS is p53. Mutant forms of p53 are found in approximately 50% of all tumors. The normal p53 protein functions as a transcription factor that can induce either cell-cycle arrest or apoptosis (programmed cell death) in response to DNA damage. FAP (choice A) is a rare inherited form of colon cancer. Germline mutations in the APC gene are responsible for FAP. All cases of neurofibromatosis (choice C) arise by inheritance of a mutant allele. Roughly 50% of all affected individuals carry new mutations, which appear to arise paternally, possibly reflecting genomic imprinting. The gene responsible for type 1 neurofibromatosis is termed NF1. Germline mutations at the NF1 locus result in multiple abnormal melanocytes 168 3: Biochemistry (café au lait spots) and benign neurofibromas. Some patients also develop benign pheochromocytomas and CNS tumors. Asmall percentage of patients develop neurofibrosarcomas, which are likely to be Schwann cell derived. Retinoblastoma (choice D) is a tumor of retinal cells, which develops in children between birth and 4 years of age. The gene responsible is termed the retinoblastoma susceptibility gene (RB) and the protein product pRB. Wilms' tumor (choice E) is a form of childhood kidney cancer. The gene responsible for this disease has been identified and is called WT1 (Wilms' tumor 1).

QUESTION 310
Which of the following clotting factors forms an active complex with tissue factor (factor III) to initiate the extrinsic clotting cascade?

A. factor I (fibrinogen)
B. factor VII (proconvertin)
C. factor VIII
D. factor IX
E. protein S

Correct Answer: B
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
The extrinsic pathway (see below figure)



is initiated at the site of injury in response to the release of tissue factor (factor III). Tissue factor is a cofactor in the factor VIIa-catalyzed (lower case alpha refers to the active form of the coagulation factors) activation of factor X. The formation of a complex between factor VIIa and tissue factor is believed to be a principal step in the overall clotting cascade. Evidence for this stems from the fact that persons with hereditary deficiencies in the components of the contact phase of the intrinsic pathway do not exhibit clotting problems. Factor VIIa, a gamma-glutamate (gla residue) containing serine protease, cleaves factor X to factor Xa in a manner identical to that of factor IXa of the intrinsic pathway. The activation of factor VII occurs through the action of thrombin or factor Xa. The ability of factor Xa to activate factor VII creates a link between the intrinsic and extrinsic pathways. An additional link between the two pathways exists through the ability of tissue factor and factor VIIa to activate factor IX. Fibrinogen (choice A) is cleaved by thrombin (factor IIa), yielding fibrin monomers that polymerize to form a fibrin clot. The activation of factor VIII (choice C) to factor VIIIa occurs in the presence of minute quantities of thrombin. Factor VIIIa is required for the activation of factor X, which represents the convergence of the intrinsic and extrinsic pathways. The activation of factor X to Xa requires assemblage of the tenase complex (C and factors VIIIa, IXa, and X) on the surface of

a^{2+}

activated platelets. As the concentration of thrombin increases, factor VIIIa is ultimately cleaved by thrombin and inactivated. This dual action of thrombin on factor VIII acts to limit the extent of tenase complex formation, and thus the extent of the coagulation cascade. Factor IX choice D) functions only in the intrinsic cascade. When activated, factor IXa aids in the activation of factor X by functioning in the tenase complex as described above. Protein S (choice E) is a cofactor for protein

C. Protein C is itself activated by thrombin and when active, cleaves factors VIIIa and Va, thus limiting the extent of the coagulation cascade.

QUESTION 311
Many effective anticancer drugs function as such by interfering with processes of DNA replication. The drug, doxorubicin, is useful in the treatment of lymphomas and breast cancers because of its ability to interfere with which of the following enzyme activities?

A. DNA ligase
B. DNA polymerase-alpha
C. primase
D. topoisomerase II
E. uracil N-glycosylase

Correct Answer: D
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Doxorubicin is a drug of the class that functions by interfering with topoisomerases. In particular, doxorubicin inhibits topoisomerase II. During the process of DNA replication ,the two strands of the DNA helix are separated. As the replication fork progresses toward sites of chromosomal attachment to the scaffold, there is an increase in the torsional stress on the helix due to supercoiling. These torsional stresses are relieved by the action of topoisomerases that introduce nicks into the DNA, which allows the strands to unwind the supercoils. Topoisomerase I introduces single-strand nicks, whereas topoisomerase II introduces double-strand nicks. Interference with the action of topoisomerases would thus impair the rate of DNA replication and this would be detrimental for rapidly proliferating cells such as cancer. Doxorubicin does not affect the activity of any of the other enzymes (choices AC, E).

QUESTION 312
Exhibit:

A. cobalamin (B_{12})
B. pantothenic acid (B_5)
C. pyridoxine (B_6)
D. riboflavin (B_2)
E. thiamine (B_1)

Please refer to the exhibit.

When fatty acids with odd numbers of carbon atoms are oxidized in the beta-oxidation pathway the final product is 1 mole of acetyl- CoA and 1 mole of the 3-carbon molecule, propionyl-CoA. In order to use the propionyl carbons, the molecule is carboxylated and converted ultimately to succinyl-CoA and fed into the TCA cycle. Which of the following represents the vitamin cofactor required in one of the steps of this conversion?

A. A
B. B
C. C
D. D
E. E

Correct Answer: A
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Propionyl-CoA is converted to succinyl- CoAin a series of reactions using three different enzymes. It is first carboxylated in an ATPdependent reaction catalyzed by propionyl- CoA carboxylase, an enzyme that requires biotin as a cofactor. The product of the first reaction, d-methylmalonyl-CoA is then converted to l-methylmalonyl-CoA by methylmalonyl-CoA racemase. Finally, methylmalonyl-CoA is converted to succinyl-CoA by the cobalaminrequiring enzyme, methylmalonyl-CoA mutase. None of the other vitamins (choice B, C, D, and E) are required in this pathway.

QUESTION 313
Mutant genes that affect several organ systems and bodily functions frequently show variable expressivity, a phenomenon referred to as phenotypic variation. The most striking example of phenotypic variability is manifest in an autosomal- dominant condition characterized by the appearance of café au lait spots on the skin and cutaneous and subcutaneous neurofibromas. These symptoms are associated with which of the following?

A. familial adenomatous polyposis
B. FH
C. Li Fraumeni syndrome
D. von Hippel-Lindau syndrome
E. von Recklinghausen disease (type I neurofibromatosis)

Correct Answer: E
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
von Recklinghausen disease (neurofibromatosis, type I), an autosomal-dominant disorder, is one of the most striking disorders that exhibits variable expressivity

(phenotypic variation). Symptoms can range from the benign appearance of café au lait spots to severe disfiguring cutaneous neurofibromas, sarcomas, and gliomas. This disorder is caused by disruption in the neurofibromin gene whose protein product functions the catalysis of inactivation of the signaling protein RAS. FAP coli (choice A) is a disorder that results in the generation of numerous small polyps in the colon by the time an individual reaches age 20. Although the polyps are asymptomatic, they are a significant contributory factor to risk and likelihood of colon cancer. This disorder is caused by mutations in the APC gene, is inherited in autosomal-dominant fashion, and its penetrance is 100% in all afflicted individuals. FH (choice B) is caused by mutations in the gene for the LDL receptor. Inheritance is autosomal dominant ith 100% penetrance. FH sufferers may be either heterozygous or homologous for a particular mutation in the receptor gene. Homozygotes exhibit grossly elevated serum cholesterol (primarily in LDLs). The elevated levels of LDLs result in their phagocytosis by macrophages. These lipidladen phagocytic cells tend to deposit within the skin and tendons, leading to xanthomas. A greater complication results from cholesterol deposition within the arteries, leading to atherosclerosis, the major contributing factor of nearly all cardiovascular diseases. LFS (choice C) is a rare form of autosomal-dominant inherited cancer caused by mutations in the tumor suppressor gene, p53. The disruption in the function of p53 leads to aberrant cell-cycle regulation and development of sarcomas, brain tumors, breast cancer, and leukemias. Cancer occurs in 50% of afflicted individuals by the time they are 30 years of age. VHL syndrome (choice D) is an inherited form of renal carcinoma that is caused by mutations in a tumor suppressor gene identified as the VHL gene.

QUESTION 314
Which of the following factors of blood coagulation is the major inhibitor of the extrinsic clotting cascade?

A. antithrombin III
B. high molecular weight kininogen
C. lipoprotein-associated coagulation factor
D. alpha-2-macroglobulin
E. protein C

Correct Answer: C
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
The major mechanism for the inhibition of the extrinsic pathway occurs at the tissue factor--factor VIIa-Ca2+-Xa--complex. The protein, lipoprotein-associated coagulation inhibitor (LACI, formerly named anticonvertin), specifically binds to this complex. LACI is composed of three tandem protease inhibitor domains. Domain 1 binds to factor Xa and domain 2 binds to factor VIIa only in the presence of factor Xa. Antithrombin III (choice A) is the most important of four thrombin regulatory proteins. This is because antithrombin III can also inhibit the activities of factors IXa, Xa, XIa, and XIIa. The activity of antithrombin III is potentiated in the presence of heparin. Heparin binds to a specific site on antithrombin III, producing an altered conformation of the protein, and the new conformation has a higher affinity for thrombin as well as its other substrates. This effect of heparin is the basis for its clinical use as an anticoagulant. The naturally occurring heparin activator of antithrombin III is present as heparan and heparan sulfate on the surface of vessel endothelial cells. It is this feature that controls the activation of the intrinsic coagulation cascade. HMWK (choice B) is important for initiation of the intrinsic pathway. When prekallikrein, HMWK, factor XI, and factor XII are exposed to a negatively charged surface, they become active. This is termed the contact phase. Exposure of collagen to a vessel surface is the primary stimulus for the contact phase. In addition to antithrombin III, thrombin activity is also inhibited by alpha-2-macroglobulin (choice D). Protein C (choice E) is activated by thrombin when thrombin is bound to thrombomodulin. Active protein C functions with its cofactor, protein S, to degrade factors VIIIa and Xa.

QUESTION 315

Regulation of iron homeostasis occurs by controlling the amount that circulates in the serum, as well as the amount contained within cells. One mechanism that plays a role in this homeostasis is iron- mediated control of the level of the intracellular iron-binding protein ferritin. Which of the following represents the mechanism of iron regulation of ferritin levels?

A. Binding of iron to ferritin leads to secretion of the complex from cells and subsequent excretion in the urine.
B. Ferritin exists as a tetramer and when iron binds, the affitinity for additional iron atoms increases.
C. Iron binds an additional protein that acts as a regulator of ferritin mRNA translation, high iron leads to increased translation and thus increased ironbinding capacity.
D. When excess iron binds to ferritin, it decreases the half-life of the protein allowing the iron to be released to the plasma and excreted.

Correct Answer: C
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
Ferritin is an iron-binding protein that prevents toxic levels of ionized iron (F) from building up in

e^{2+}

cells. As iron levels increase, the need to increase the amount of ferritin also increases. Iron-mediated regulation of ferritin levels occurs through the action of an iron response element-inding protein (IRBP) that binds to specific iron response elements (IREs) in the 5'-UTR of the ferritin mRNA. These IREs form hairpin loop structures that are recognized by IRBP. This IRBP is an iron-deficient form of aconitase, the iron-requiring enzyme of the TCA cycle. When iron levels are high, IRBP cannot bind to the IRE in the 5'-UTR of the ferritin mRNA. This allows the ferritin mRNA to be translated. When iron levels are low, IRBP is free of iron and can therefore, interact with the IRE in the ferritin mRNA preventing its translation. Binding of iron by ferritin does not increase its excretion in the urine (choice A). Ferritin does not exist as a multimeric protein exhibiting iron binding cooperativity (choice B). Iron binding to ferritin does not affect the halflife of ferritin (choice D).

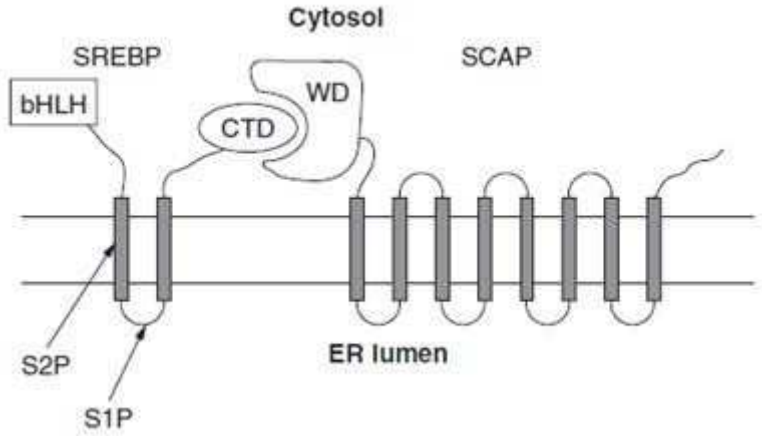
QUESTION 316
Regulation of cholesterol, fatty acid, phospholipid, and triglyceride synthesis is controlled in part by the level of sterols. These sterol-regulated biosynthesis pathways involve a unique family of transcription factors that are best described by which of the following?

A. Binding of sterols to these factors induces a conformational change preventing interaction with RNA polymerase.
B. They are membrane-bound proteins and only released on activation of a sterolregulated protease.
C. They contain zinc fingers that bind sterols leading to their activation.
D. They require interaction with sterols, much like steroid hormone receptors, prior to binding to DNA.
E. On sterol binding, these factors are recognized by the proteosome and thus targeted for degradation.

Correct Answer: B
Section: Biochemistry

Explanation

Explanation/Reference:
Explanation:
The continual alteration of the intracellular sterol content occurs through the regulation of key sterol synthetic enzymes, as well as by altering the levels of cell-surface LDL receptors. As cells need more sterol they will induce their synthesis and uptake, conversely when the need declines synthesis and uptake are decreased. Regulation of these events is brought about primarily by sterol-regulated transcription of key rate-limiting enzymes and by the regulated degradation of HMGR. Activation of transcriptional control occurs through the regulated cleavage of the membrane- bound transcription factor SREBP (there are three SREBPs). Sterol control of transcription affects more than 30 genes involved in the biosynthesis of cholesterol, triacylglycerols, phospholipids, and fatty acids. Transcriptional control requires the presence of an octamer sequence in the gene termed the sterol regulatory element, SRE-1. It has been shown that SREBP is the transcription factor that binds to SRE- 1 elements. All three SREBPs are proteolytically regulated by sterols. Full-length SREBPs have several domains and are embedded in the membrane of the ER. The N-terminal domain contains a transcription factor motif of the basic helix-loop-helix (bHLH) type that is exposed to the cytoplasmic side of the ER (see below figure). When sterols are scarce, cleavage of the full-length SREBP takes place with the result being that the N-terminal bHLH motif is released into the cytosol. The bHLH domain then migrates to the nucleus to direct transcription. Conversely, when sterols are abundant, cleavage of SREBP is inhibited. To control the level of SREBP-mediated transcription, the soluble bHLH domain is itself subject to rapid proteolysis. The cleavage of SREBP is carried out by two distinct enzymes, one of which is regulated by sterols. The regulated cleavage occurs in the lumenal loop between the two transmembrane domains. This cleavage is catalyzed by site-1 protease, S1P. High sterol content blocks the activity of S1P. The second cleavage, catalyzed by site-2 protease, S2P, occurs in the first transmembrane span, leading to release of active SREBP. In order for S2P to act on SREBP, site-1 must already have been cleaved. Additional studies on sterol-regulated gene expression demonstrated that cleavage of SREBP by S1P is controlled by the level and action of an additional protein termed, SREBP leavage-activating protein, SCAP.



SCAP is a large protein also found in the ER membrane and contains at least eight transmembrane spans. The C-terminal portion, which extends into the cytosol, has been shown to interact with the C- terminal domain of SREBP. This C-terminal region of SCAP contains four motifs called WD40 repeats. The WD40 repeats are required for interaction of SCAP with SREBP. The function of SCAP is to positively stimulate S1P-mediated cleavage of SREBP. The function of sterols is to inhibit this positive action of SCAP. The activity of SCAP involves movement from the ER to the Golgi and back. Because the C-terminus of SCAP interacts with SREBP, movement of SCAP takes SREBP along for the ride. When sterols are low, SCAP and SREBP move to the Golgi. This transit is required for SREBP

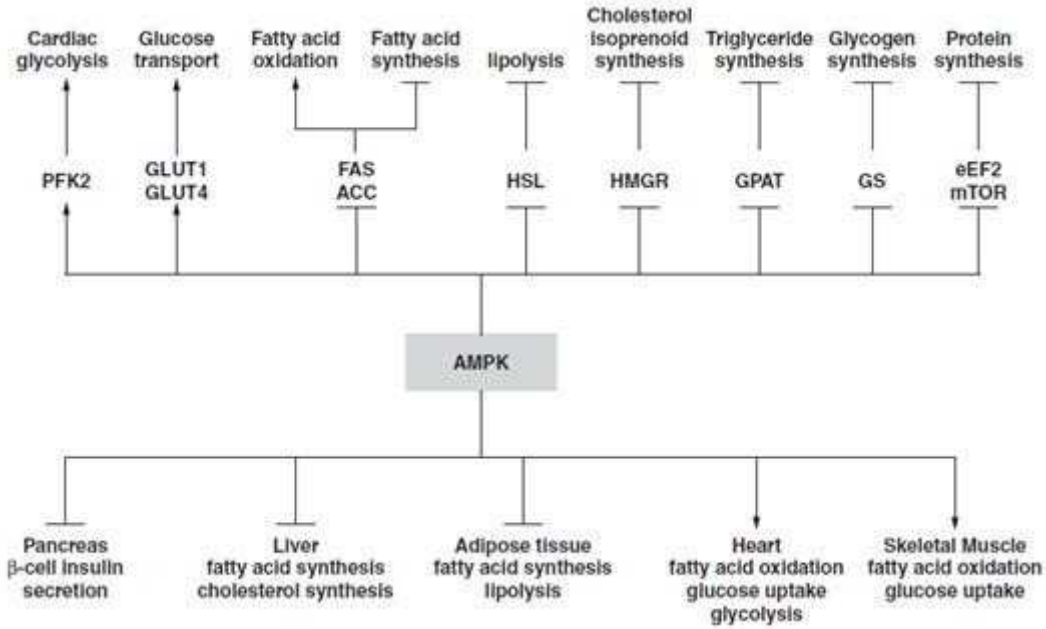
cleavage as S1P is Golgi-localized. When sterols are high, movement of SCAP is halted. Thus, the overall effect of sterols is to regulate the ability of SCAP to present SREBP to S1P. None of the other choices (A, CE) represent the mechanisms of sterol-mediated regulation of gene expression.

QUESTION 317
Metformin is one of the most prescribed hypoglycemia-inducing drugs in the treatment of Type II diabetes. One of the effects of metformin is a reduction in adipose tissue lipolysis, which is effected via the activation of AMP-activated kinase (AMPK). Which of the following actions of AMPK explains the adipose tissue benefits of metformin?

A. activation of ACC
B. activation of FAS
C. inhibition of hormone-sensitive lipase
D. inhibition of mammalian target of rapamycin (mTOR)
E. inhibition of 6-PFK-2

Correct Answer: C
Section: Biochemistry
Explanation

Explanation/Reference:
Explanation:
AMP-activated protein kinase (AMPK) was first discovered as an activity that inhibited preparations of ACC and 3-hydroxy-3-methylglutaryl- CoA reductase (HMG-CoA reductase, HMGR) and was induced by AMP. AMPK induces a cascade of events within cells in response to the ever changing energy charge of the cell. The role of AMPK in regulating cellular energy charge places this enzyme at a central control point in maintaining energy homeostasis (see below figure). Once activated, AMPK- ediated phosphorylation events switch cells from active ATP consumption (e.g., fatty acid and cholesterol biosynthesis) to active ATP production (e.g., fatty acid and glucose oxidation). Other important activities attributable to AMPK are regulation of insulin synthesis and secretion in pancreatic islet beta-cells. As shown in



AMPK inhibits (not activates) both ACC (choice A) and FAS (choice B). Activation (not inhibition) of PFK-2 (choice E) occurs in response to AMPK. Although AMPK does indeed inhibit mTOR (choice D), this inhibition does not have any influence on adipose tissue lipolysis.

QUESTION 318
The protein encoded by the APC gene is a tumor suppressor the role of which is to regulate the activity of cellular signaling induced by the Wnt growth factor. Therefore, loss of APC activity is associated with unrestrained cellular proliferation. Which of the following signaling molecules is the target for APC interaction?

A. beta-catenin
B. MYC
C. p53
D. pRB
E. von Hippel-Lindau protein (pVHL)

Correct Answer: A
Section: Biochemistry
Explanation

Explanation/Reference:

Explanation:
The protein of the Wnt signaling cascade, to which APC associates, is beta-catenin. Using antibodies specific for the NH2-terminus of APC, it was possible to coprecipitate additional PCassociated proteins leading to the identification that one of these APC-associated proteins was beta-catenin. The catenins are a family of proteins that interact with the cytoplasmic portion of the cadherins (cell-cell adhesion family of proteins), thus linking the cadherins to the actin cytoskeleton. Catenins are equally important in the signaling cascade initiated by the Wnt family of proteins that are involved in embryonic patterning, development of the nervous system. The Wnt proteins are secreted factors that interact with cell-surface receptors. Wntreceptor interaction induces the activity of the cytoplasmic phosphoprotein dishevelled. Activated dishevelled inhibits the serine/ threonine kinase glycogen synthase kinase-3- beta (GSK-3). When GSK-3-beta is inhibited, beta-catenin becomes hypophosphorylated. The hypophosphorylated form of beta-catenin migrates to the nucleus and interacts with transcription factors, thereby, inducing expression of various genes. The role of APC in this pathway is to bind phosphorylated beta-catenin. The APC-beta-catenin complex stimulates the breakdown of beta-catenin. Therefore, mutations that lead to a loss of APC, or to a loss of the portion of the APC protein that interacts with beta-catenin, would lead to constitutive activation of several genes that could then promote the transformed phenotype. None of the other proteins (choices BE) are known to interact with APC.

QUESTION 319
A student has a genetic defect and cannot produce the J chain which is important in the structure of some immunoglobul in molecules. Which of the following will most likely be observed in this individual?

A. a decrease in mature B cells
B. a decrease in mature T lymphocytes
C. a decrease in serum IgM
D. an increase in IgA in the intestine
E. an increase in serum IgM and decrease in IgE

Correct Answer: C
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
Deficiency in production of J chains for immunoglobulins could result in a decrease in serum IgA and IgM levels. These antibodies are dimers and pentamers, respectively, of the basic immunoglobulin molecule, and require a J chain to join the immunoglobulin chains. There is no evidence which indicates that a deficiency in the production of J chains of IgA or IgM will cause a decrease in mature B cells, or T lymphocytes, an increase in serum IgM and decrease in IgE, or a decrease in IgA (choices A, B, D, and E).

QUESTION 320
A 10-year-old boy has a bacterial pneumonia. The etiologic agent had M type-1 protein and grew on blood agar. The patient's immune system appeared incapable of controlling the infection. Adecrease in which of the following is most directly related to the immunological failure?

A. antibody activity
B. cytotoxic T-cell function
C. IL-4 and IL-10 levels
D. mast cell degranulation
E. platelet aggregation

Correct Answer: A
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
A deficiency in immunoglobulin production or activity is directly related to susceptibility to common extracellular microbes such as streptococci. Cytokines such as the interleukins, IL-4 and IL-10 (choice C), the function of T cells (choice B) or mast cells (choice D), and nonantibody factors (choice E) are not directly involved in increased susceptibility to bacterial infections.

QUESTION 321
An emaciated prisoner in a New York prison began coughing up sputum streaked with blood. Examination of the sputum revealed the presence of acid-fast bacilli. Which of the following would be least helpful in establishing a diagnosis of tuberculosis?

A. agglutination test for antibodies
B. niacin production test
C. nitrate reduction test
D. rough, non-pigmented colonies
E. slow growth on Lowenstein-Jensen medium

Correct Answer: A
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
Molecular amplification techniques provide fast diagnostic results when they are compared to traditional cultural procedures for M. Tuberculosis, which often has to be incubated for several weeks. The rod-shaped, aerobic bacteria do not stain readily, but once stained they resist decoloration by acid or alcohol (hence, acid-fast bacilli). Cellular immunity is most important in how a host controls the growth and spread of the tubercle bacteria. There is evidence that mononuclear phagocytes ingest the organisms and even destroy them. The tuberculin skin test is based on cellular immune mechanisms, with the PPD causing a positive skin reaction in a person who has encountered the mycobacterium in the past. As a result, humoral immunity reactions are of little use diagnostically (choice A). Other mycobacteria are capable of accumulating niacin (choice B) and reducing nitrate (choice C). The development of rough, non-pigmented colonies on media (choice D) and slow growth on L-J medium (choice E) are also not specific for M. tuberculosis since slow growth (weeks) and colony morphology (rough, no pigment) are characteristic

of other species of Mycobacterium.

QUESTION 322
Following the consumption of fish at a local restaurant, a 17-year-old girl suddenly experiences severe dyspnea. Upon arrival at the local emergency room she is found to be severely hypotensive and in respiratory distress. Urticarial wheals are also noted all over her body. As the resident physician you quickly realize this to be a hypersensitivity reaction. To which of the following immunoglobulins does the allergen bind rapidly during the activation stage of mast cells?

A. IgA
B. IgD
C. IgE
D. IgG
E. IgM

Correct Answer: C
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
Within seconds after the allergen encounters human tissue, it binds to IgE antibodies which are attached to mast cells. When it engages at least two IgE molecules it forms a bridge between them. This cross-linking, in turn, draws the attached IgE receptors close to one another. Such aggregation of receptors activates mast cells to release histamine and other vasoactive substances that generate the allergic reaction. IgA, IgG, IgM, or IgD are not the germane antibodies to which allergens bind (choices A, B, D, and E).

QUESTION 323
Physical examination reveals severe laryngeal edema resulting in a marked hoarseness when the 17- year-old girl attempts to speak. Also, her lips and tongue show significant swelling. Which of the following chemicals most likely caused this edematous swelling?

A. corticosteroids
B. cromolyn sodium
C. epinephrine
D. histamine
E. 5-lipoxygenase

Correct Answer: D
Section: Microbiology/Immunology
Explanation

Explanation/Reference:

Explanation:
Histamine is among the class of preformed (primary) mediators released from mast cells upon degranulation and is classified as a biogenic amine. It is a potent pharmacologically active substance that can dilate small blood vessels and increase vascular permeability, allowing fluid to leak into tissues. These vascular changes can give rise to swelling and redness. Histamine can stimulate production of mucus from the epithelium, thus contribute to congestion of airways. It can cause smooth muscles around the bronchial airways and the intestine to contract. Prostaglandins and leukotrienes like histamine can also cause constriction of the bronchial tubes and vascular dilation. Corticosteroids are anti-inflammatory drugs that are used for the treatment of asthma, autoimmune diseases, or graft rejection (choice A). Epinephrine and cromolyn sodium counteract the action of histamine or other mediators of type I hypersensitivity reaction and are used for the treatment of anaphylactic reactions (choices B and C). 5- lipoxygenase retards production of several leukotrienes (choice E).

QUESTION 324
In February, three patients from a nursing home in East Dallas develop an abrupt onset of a febrile upper respiratory tract illness. They have received no immunizations in the last year. Culture of the nasopharynx of one patient shows influenza A virus. To prevent further cases within the next two weeks, which of the following should be administered?

A. acyclovir
B. amantadine
C. hyperimmune serum globulin
D. influenza A vaccine
E. ribavirin

Correct Answer: B
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
Influenza viruses are helical viruses with a segmented, negative-sense RNA genome. A, B, and C types are determined by the protein coat of the virus. The infections are characterized by short (12 days) incubation periods and are efficiently transmitted in respiratory secretions. While most RNA viruses grow only in the infected cell cytoplasm, influenza viruses have growth steps in both the cytoplasm and nucleus of the host cell. The patient's humeral immune system is most important in controlling virus growth. The important antibodies are made against the viral hemeagglutinin (early viral attachment) and the NA (release of mature viruses) enzymes. Amantadine (choice B) and rimantadine block viral uncoating and must be given prophylactically. Oseltamivir (Tamiflu) inhibits NA activity and must also be given before viral infection for best results. Acyclovir (choice A) is an antiherpetic drug. Passive immunity (choice C) does not play a significant role in influenza control. Ribavirin (choice E) is used to treat RSV, a paramyxovirus. Active immunity (choice D) is the most effective mechanism of controlling influenza on a population basis and probably would not be as effective as prophylactic antivirals in the nursing home arena.

QUESTION 325
Which of the following statements best describes interferon's suspected mode of action in producing resistance to viral infection?

A. It alters the permeability of the cell membrane so that viruses cannot enter the cell.
B. It stimulates a cell-mediated immunity.

C. It stimulates humoral immunity.
D. Its action is related to the synthesis of a protein that inhibits mRNA function.
E. Its direct antiviral action is related to the suppression of messenger RNA formation.

Correct Answer: D
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
Interferons are produced by most nucleated cells in the body, and inhibit the translation of viral proteins. There are three major types of interferons, that is, alpha, beta, and gamma. Interferons are active against many viruses and are not specific. Virus infection in one cell induces interferon production which moves to an adjacent, uninfected cell and causes an antiviral protein (AVP) to be produced by the second cell. This AVP inhibits viral mRNA activity and thereby inhibits viral protein production. Interferons do not destroy viruses, but probably result in fewer virions that need to be eliminated by the host's immune system. Interferons do not affect host cell membranes (choice A) or directly suppress mRNA function (choice E). Interferons do not directly stimulate either cellular (choice B) or humoral (choice C) immunity to enhance an antiviral effect.

QUESTION 326
A 25-year-old man with acquired immune deficiency disease (AIDS) has malabsorption, chronic abdominal pain, low-grade fever, and nonbloody diarrhea. In fecal smears, large numbers of oocysts containing four sporozoites were observed. Which of the following organisms is most likely the etiological agent?

A. Cryptosporidium parvum
B. Entamoeba histolytica
C. Giardia lamblia
D. Microsporidia species
E. Taenia solium

Correct Answer: A
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
All five organisms are protozoa. There are two intestinal protozoa specifically associated with AIDS that can cause transient diarrhea in immunocompetent individuals, but can cause debilitating, and potentially life-threatening, chronic diarrhea in AIDS patients. These organisms are C. parvum with no effective drug therapy, and Isospora belli treated with folate antagonists, such as trimethoprim- sulfamethoxazole. Microsporidia may cause severe, persistent, watery diarrhea in AIDS patients, but they produce spores rather than oocysts (choice D). T. solium is the pork tapeworm which occasionally may cause diarrhea (choice E). E. histolytica and G. lamblia may cause diarrhea, but they are not closely associated with AIDS (choices B and C).

QUESTION 327

A 38-year-old sexually-active woman developed symptoms of lower abdominal pain with adjacent tenderness. No gram-negative cocci were observed or isolated. The obligate intracellular organism causing the infection is unable to perform which of the following metabolic functions?

A. form ATP
B. form the intracellular, metabolically active, reticulate body
C. produce polypeptides
D. reproduce by binary fission
E. synthesize DNA gyrase

Correct Answer: A
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
Chlamydae are obligate intracellular parasites because they cannot synthesize ATP. They are classified as bacteria because they divide by binary fission (choice D), form polypeptides (choice C), produce RNA, DNA, and DNA gyrase (choice E). Finally, they synthesize two unique morphological forms. That is, the extracellular infective, metabolically inert elementary body, and the intracellular, metabolically active reticulate body (choice B).

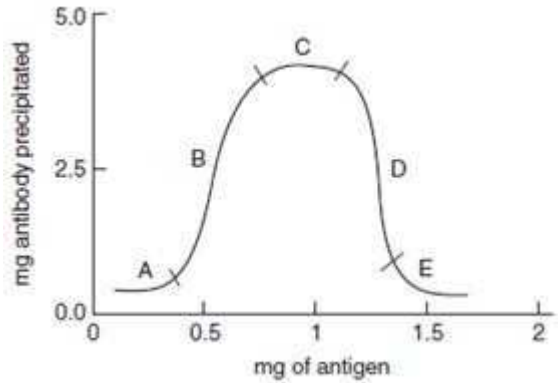
QUESTION 328
Severe septic infections caused by bacteriapossessing capsules often occur following splenectomy. Which of the following statements most accurately explains why this medical complication is able to occur?

A. The spleen is a source of IgM and IgG antibodies needed to opsonize encapsulated bacteria.
B. The spleen is the main source of stem cells.
C. The spleen is uniquely equipped to process capsular polysaccharides.
D. The spleen rapidly inactivates many antimicrobial agents.
E. The spleen readily metabolizes therapeutic doses of antibiotics.

Correct Answer: A
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
The spleen is important for the production of IgM and IgG antibodies needed to opsonize encapsulated bacteria. Involvement of the spleen in metabolizing (choice D), inactivating of antimicrobial agents (choice E), or processing of capsular polysaccharides (choice C) is not considered important. The main source of stem cells is the bone marrow not the spleen (choice B).

QUESTION 329
Below figure shows a quantitative precipitin curve of an antigen-antibody reaction, where the amount of antibody is kept constant throughout. According to the figure, which of the following statements is correct?



A. point A shows antigen excess
B. point B shows that there is no antibody formation
C. point C indicates that there is little, if any, free antigen and antibody in the reaction tube
D. point D represents the area of antigen destruction
E. point E indicates antibody excess

Correct Answer: C
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
Point C represents the zone of equivalence, that is, that point of the antigen-antibody reaction when optimal concentrations of antigen and antibody combine. Thus, there is little, if any, free antigen and antibody, and as a consequence maximal amounts of antigen and antibody will be found in the precipitate resulting from the antigen-antibody reaction. Points A and B represent areas in the antigen- antibody precipitin curve where there is an excess of antibody (choices A and B). Points D and E show areas in the precipitin curve where there is an antigen excess in the antigen-antibody reaction mixture (choices D and E).

QUESTION 330
A newborn boy appears to be lethargic and septic. Aspinal tap was performed, and a Gram stain of the spinal fluid revealed gram-positive bacilli. Cultures of the spinal fluid on sheep blood agar plates, at a temperature of 2225℃, yielded catalase-positive hemolyt ic rods that had a tumbling motion. Penicillin cleared the infection. Which of the following is the most likely organism that caused this disease?

A. Bacillus cereus
B. Bordetella pertussis
C. Corynebacterium diphtheria
D. Listeria monocytogenes
E. Neisseria meningitidis

Correct Answer: D
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
L. monocytogenes causes meningitis and sepsis in newborns and patients whose immune systems have been compromised by irradiation or chemotherapy. When this microbe is growing at a temperature of 2225℃ on blood agar, it yields gram-positive rods, which move with a characteristic tumbling motion. A slight zone of hemolysis surrounds the colonies of L. monocytogenes. These characteristics are not applicable to B. cereus (choice A), B. pertussis (choice B), N. meningitides (choice E), or C.
diphtheriae (choice C).

QUESTION 331
A 25-year-old female presents to her doctor's office with a rash over the malar eminences of her face, sparing the nasolabial folds; a skin rash due to exposure to sunlight; and painless nasopharyngeal ulcers. Suspecting an autoimmune disorder, her physician obtains an antinuclear antibody test of her blood and finds high titers of anti-double-stranded DNA antibodies. Which one of the following diseases is most likely responsible for this immunological reaction?

A. Goodpasture syndrome
B. multiple sclerosis
C. myasthenia gravis
D. rheumatoid arthritis
E. systemic lupus erythematosus

Correct Answer: E
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
SLE is characterized by development of auto-antibodies against double-stranded DNA, and other components of the nucleus. These auto-antibodies are involved in the production of immune complexes that lead to activation of complement, tissue damage, including vasculitis, glomerulonephritis, or arthritis. Rheumatoid arthritis (choice D) is due to production of auto-antibodies (of the IgM type) against IgG. In multiple sclerosis (choice B), auto-activated T cells and macrophages cause demyelization of the white matter of the brain. Goodpasture syndrome (choice A) is caused by the development of auto-antibodies to the collagen component of the

basement membrane of the lungs and kidneys. In myasthenia gravis (choice C), auto-antibodies are generated against the acetylcholine receptors of the neuromuscular junction.

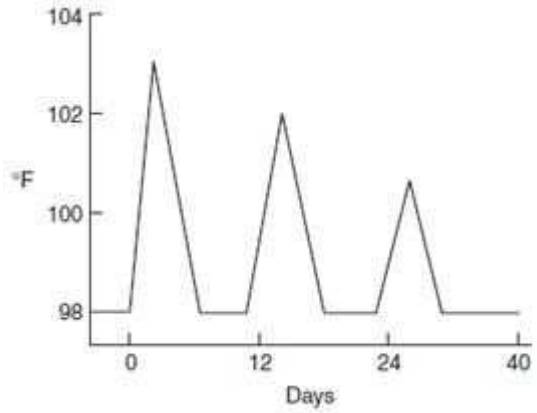
QUESTION 332
Administration of which one of the following substances is likely to be most beneficial to this patient?

A. gamma interferon
B. interleukin-1
C. plasmapheresis
D. prednisone
E. tumor necrosis factor (TNF)

Correct Answer: D
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
Prednisone alone or in combination with methotrexate and azathioprime is commonly used for the treatment of systemic lupus erythematosus. The cytokines TNF (choice E), interleukin-1 (choice B), or gamma interferon (choice A) have not been shown to be effective against SLE. Plasmapheresis (choice C) has been used for the treatment of Guillain-Barre syndrome and myasthenia gravis

QUESTION 333
Amedical student was bitten by infected ticks. In a week, he developed a high fever, headache, muscular aches, nausea, and splenomegaly. Five days later his symptoms subsided. However, 1 week later all his previous symptoms returned. During the next 9 days he went through a recovery and another relapse followed by a final recovery. The overall temperature curve of his illness is shown in below figure. Which of the following is the most likely etiological agent?



A. Borrelia burgdorferi
B. B. recurrentis
C. Leptospira interrogans
D. T. carateum
E. T. pertenue

Correct Answer: B
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
The endemic form of relapsing fever is transmitted by ticks infected by B. recurrentis. Relapsing fever begins with headache, high fever, muscle aches, and splenomegaly. It has a unique fever curve due to the emergence of various antigenic types of B. recurrentis. B. burgdorferi (choice A) causes a distinct spreading circular rash with a clear center, which is called erythema chronicum migrans. L. interrogans (choice C) is transmitted by rat urine and causes leptospirosis. This disease is associated with jaundice, uremia, and aseptic meningitis. T. carateum (choice D) is the cause of pinta, which is characterized by hyperpigmentation of the skin. T. pertenue (choice E) is transmitted by contact with infected persons and is characterized by the development of cauliflowerlike skin lesions.

QUESTION 334
A 7-year-old boy experienced respiratory tract inflammation, sore throat, and fever. Labored breathing soon followed the development of a gray membrane in the tonsil area, and diphtheria was diagnosed. Which of the following represents the most immediate course of action by his physician?

A. acid-fast stain of a throat specimen
B. culture of a throat specimen on blood agar
C. injection of diphtheria antitoxin
D. oral administration of sulfonamides
E. performance of a spinal tap

Correct Answer: C
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
A physician is justified in giving antitoxin on clinical evidence, or suspicion of diphtheria, without waiting for laboratory confirmation. The antitoxin dosage should be adjusted according to the weight of the patient and the severity of the infection. The antitoxin is given to neutralize free diphtheria exotoxin in the body fluids and timeliness is of extreme importance. Once the exotoxin has been bound by the body cells and exerted its influence, diphtheria antitoxin is of little value. C. diphtheria localizes in the throat, and thus spinal taps are useless (choice E). Tellurite agar, not blood agar, is used for the isolation of C. diphtheriae from throat

swabs, because it is a selective medium for this germ, inhibiting the growth of other bacteria present in throat swabs (choice B). C. diphtheriae is not an acid-fast microbe. Methylene blue is used to stain smears for the bacteriological diagnosis of diphtheria (choice A). This initial treatment of choice for diphtheria is antitoxin. Treatment with penicillin G or erythromycin, but not sulfonamides, may be used. Penicillin G or erythromycin are not substitutes for diphtheria antitoxin (choice D).

QUESTION 335
An 8-month old boy presents to the emergency room in respiratory distress from a recurrent upper respiratory tract bacterial infection. Labs reveal low levels of IgA, IgD, IgE, IgG, and IgM. Suspecting animmune deficiency disorder, genetic testing reveals a defect in a tyrosine kinase gene. Which of the following would be seen in patients with this immune deficiency disorder?

A. particular susceptibility to viral and fungal infections
B. profound deficiencies of cell-mediated immunity
C. depletion of lymphocytes in the paracortical areas of lymph nodes
D. normal numbers of B lymphocytes
E. very low quantities of immunoglobulin in their serum

Correct Answer: E
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
Bruton hypogammaglobulinemia is a B-cell immunodeficiency disorder that is X-linked recessive and thus only affects males (boys). Affected patients are deficient in B cells in the peripheral blood and in B-dependent areas of lymph nodes and spleen. Most of the serum immunoglobulins are absent, and the IgG level is <200 mg/L. Recurrent pyogenic infections usually begin to occur at 56 months of age, when maternal IgG has been depleted. Individuals with Bruton syndrome have normal T-cell-mediated immune responses (choice B). Patients suffering from X-linked hypogammaglobulinemia do not have normal numbers of B lymphocytes, because the pre-B cells from which B cells are produced fail to differentiate into B cells. This is due to a gene mutation in pre-B cells, which does not allow pre-B cells to form tyrosine kinase (choice D). The number of lymphocytes in the paracortical areas of lymph nodes of patients with Bruton syndrome is normal (choice C). Individuals with X-linked hypogammaglobulinemia have normally functioning T cells, and thus are not particularly susceptible to viral or fungal infections, which are dependent on proper T-cellmediated immune responses (choice A).

QUESTION 336
During a pelvic examination, a woman is found to have painful vesicular lesions on the vagina. The patient states that she had similar lesions 12 months previously which lasted for 2 weeks. Which of the following is the most likely causative agent?

A. cytomegalovirus
B. herpes simplex virus
C. papillomavirus
D. rubella virus
E. varicella virus

Correct Answer: B
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
Recurrent vesiculating lesions in the genital region suggest human herpesvirus type II, although type I is seen in some cases. Choice B would be the correct answer. Cytomegalovirus (choice A) and rubella virus (choice D) will commonly form latent infections but would not appear as vesicular lesions in the genital area if reactivated. Rubella may occur as a macular rash on the skin, but only in the initial infection episode. Papillomaviruses (choice C) are highly tropic for epithelial cells of the skin and mucus membranes. Papilloma lesions (warts) are benign except for certain strains and are never presented as vesicular. Warts contain lesion parts known as the horny layer and the granular layer. Varicella (choice E) or chickenpox will usually have all stages of a lesion (macule, papule, vesicle, and pustule) present and would be skin lesions, not in the genital mucus membrane area of the body.

QUESTION 337
Antibodies against acetylcholine neural receptors were measured in a 35-year-old woman and are thought to be involved in the pathogenesis of which of the following?

A. acute idiopathic polyneuritis
B. Guillain-Barr syndrome
C. multiple sclerosis
D. myasthenia gravis
E. postpericardiotomy syndrome

Correct Answer: D
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
Anti-acetylcholine receptor antibodies are found in more than 90% of myasthenia gravis patients. If the clinical symptoms are suggestive of myasthenia gravis, this finding alone is often considered diagnostic. Multiple sclerosis patients tend to have high levels of measles virus antibodies in their spinal fluid. However, the role of this agent in the disease is undetermined (choice C). Guillain-Barr syndrome (also called acute idiopathic polyneuritis) is a demyelinating disease of peripheral nerves. It commonly occurs after a viral infection or an injection, such as influenza immunization. The disease seems to be caused by a T-cell response to nervous tissue (choices A and B). Postpericardiotomy syndrome is a term used to describe a disorder following surgery of the pericardium to remove cysts or tumors or to correct a malformation (choice E).

QUESTION 338
Which of the following will be observed in a person who is deficient in interleukin-1 synthesis?

A. difficulty with immunoglobulin isotypic switching
B. dependence on endotoxin for the induction of febrile responses
C. effective mediation of acute phase responses
D. effective regulation of vascular shock
E. tendency to develop intense inflammatory reactions

Correct Answer: B
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
Interleukin-1 (IL-1) is a protein generated primarily by macrophages. The cytokine is called endogenous pyrogen because it acts on the hypothalamus to produce fever during infections and inflammatory conditions. Thus individuals who are unable to produce IL-1 most likely will have to depend on endotoxin, the exogenous pyrogen, to induce febrile reactions. Mediation of immunoglobulin isotypic switching (choice A) requires IL-4 and IL-5. Acute-phase responses (choice C) and shock (choice D) are mediated by IL-6 and TNFalpha, TNF-alpha. Intense inflammatory reactions are produced by IL-1 (choice E).

QUESTION 339
After an abdominal surgery for removal of ovarian cysts, a 56-year-old female has had low-grade fever for the past 2 weeks. She has a history of rheumatic fever as a child. Three of the blood cultures grew gram-positive cocci. Which of the following is the most likely etiologic agent?

A. Group A streptococci
B. group B streptococci
C. group C streptococci
D. group D streptococci
E. S. viridans

Correct Answer: D
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
There are at least 12 species of enterococci, and all are classified as group D streptococci (choice D). E. faecalis is the most common and causes 8590% of enterococcal infections. As long as enterococci remain in the intestinal tract, they are seldom involved in disease. Yet, they are extremely efficient opportunists. The enterococci are among the most frequent causes of nosocomial infections, especially in intensive care units. They are commonly found in complications of intra-abdominal surgery, often as part of a mixed culture of microorganisms. Antibiotic therapy (cephalosporins, etc) is often a selective feature since enterococci are resistant to many of the antimicrobials in common use. Group Astreptococci (choice A) would be represented by S. pyogenes and is the group which causes about 95% of human infections (skin, septicemia, organs, etc), but would seldom be found in intra-abdominal complications. Streptococci B (choice B) are most often

found in infections of infants since type B streptococci are found routinely in the vaginal flora. Group C streptococci (choice C) usually occur in the nasopharynx and may cause sinus, blood, or heat infections. S. viridans (choice E) are usually found in the oral cavity and may be opportunists involving blood and heart infections.

QUESTION 340
Aurease-positive, spiral-shaped gram-negative rod is found in gastric washings from a 29-year-old stressed-out medical student with gastritis. Which of the following is most likely to be this organism?

A. Campylobacter jejuni
B. Helicobacter pylori
C. Proteus mirabilis
D. Providencia rettgeri
E. Vibrio cholerae

Correct Answer: B
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
H. pylori is a spiral-shaped gram-negative motile rod that is associated with antral gastritis and duodenal (peptic) ulcer disease. It is oxidase-positive, catalase-positive, and a strong producer of urease. Antimicrobial therapy that clears H. pylori results in improvement of gastritis and duodenal ulcer disease. Hence, choice B is the correct answer. C. jejuni (choice A) infections are widespread and usually cause abdominal pain and profuse bloody diarrhea, not gastritis and ulcer manifestations. Ureasepositive P. mirabilis (choice C) and other Proteus species produce infections in humans when the bacteria leave the intestinal tract, being very significant in urinary tract and bacteremia infections. P. retteri (choice D) is a member of the normal intestinal flora, often resistant to antimicrobial therapy, and is seen in urinary tract infections. V. cholerae is a comma-shaped curved rod and is widely distributed in marine and surface waters in nature. It is oxidase positive and many species are salt tolerant. V. cholerae (choice E) produces a heat-labile enterotoxin whose action increases cAMP in intestinal cells, resulting in prolonged hypersecretion of water and electrolytes.

QUESTION 341
A 3-year-old child arrives at the hospital in severe respiratory distress. Periorbital edema is also noted. Blood analysis reveals decreased levels of C4 and decreased levels of C1 inhibitor. This complement deficiency is likely to lead to which of the following conditions?

A. angioedema
B. an increased susceptibility to pyogenic infections
C. bacteremia
D. decreased production of anaphylatoxins
E. enhancement of antibody production

Correct Answer: A
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
Deficiency in the inhibitor of the first component of complement (C1) is associated with angioedema, because this condition leads to the production of anaphylatoxins C3a, C4a, and C5a. These anaphylatoxins act on mast cells, which release large amounts of histamine. Production of histamine increases capillary permeability resulting in edema. Enhanced susceptibility to pyogenic infections has been attributed to C3 and C5C8 components of complement. Bacteremia is a term used to indicate the presence of bacteria in the blood. Thus it has nothing to do with the first component of complement (choice C). Inherited deficiencies of C3 and C5C8 have been associated with increased susceptibility to pyogenic infections, but not the first component of complement (choice B). Complement can act synergistically with antibody to modify its action, but not its production (choice E). The conversions of the third (C3) and fifth (C5) components of complementby the C3 and C5 convertases to C3a and C5a anaphylatoxins lead to the increased production of anaphylatoxins (choice D) seen with C1 inhibitor deficiency.

QUESTION 342
A rabbit is repeatedly injected with a peptide hapten. Two weeks later, its serum is subjected to a gel diffusion assay with the hapten and a carrier protein. Which of the following would be the expected result of the gel diffusion assay?

A. A line of identity between serum and both the carrier and the hapten will be present.
B. A line of identity between the serum and carrier protein will be detected.
C. A line of nonidentity between serum, carrier, and hapten will be detected.
D. A line of partial identity between serum, carrier, and hapten will be detected.
E. No precipitin line will be present.

Correct Answer: E
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
By definition, a hapten is a substance of low molecular weight that by itself does not elicit the formation of antibodies. However, when attached to a carrier protein, antibody production becomes possible. The haptencarrier approach has been employed to produce antibodies against penicillin, steroids, nucleotides, lipids, and even 2,4-dinitrophenol. Since the rabbit has been repeatedly injected with the hapten only, the serum cannot be expected to have antibodies against the hapten. It

is clear that when the serum is subjected to a gel diffusion assay with the hapten and a carrier protein not used to complex the hapten during immunization, no antigen-antibody precipitin lines of either identity, partial identity, or nonidentity can be expected to form (choices A, B, C, and D).

QUESTION 343
A 45-year-old male experiences memory lapses, loss of reasoning ability, ataxia, and myoclonic jerking. His condition steadily deteriorates and finally progresses to stupor, coma, and death. The physician notes that 34 years ago, the patient was given injections of growth hormone prepared from human pituitary glands. Histological sections of brain show widespread neuron loss, vacuolation, and inflammation. Which of the following is the most likely diagnosis?

A. Creutzfeldt-Jacob disease (CJD)
B. kuru
C. meningitis due to herpes simplex virus
D. progressive multifocal leukoencephalopathy (PML)
E. subacute sclerosing panencephalitis (SSPE)

Correct Answer: A
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
CJD (choice A) is caused by a prion, a protein agent with no detectable nucleic acid for a genome. It is considered to be one of a group of degenerative central nervous diseases called transmissible spongiform encephalopathies. Its incubation period most often lasts for years. CJD in humans begins gradually, with progressive dementia, ataxia, twitching of muscles (myoclous), and leading to death within a year. While cases are rare, there may be some type of familial association. Kuru (choice B) is similar to CJD but was confined to New Guinea. Once consumption of dead relatives was outlawed, the disease disappeared. Herpes simplex meningitis (choice C) results in a fairly rapid onset of symptoms caused by destructionof brain tissue, followed by a mortality rate of 7580%. Acyclovir treatment is usually beneficial. PML (choice D) is caused by JC Virus (JCV), a polyomavirus. It is considered a slow virus disease. Several polyomaviruses are important DNA tumor viruses. PML is seen in about 5% of patients with AIDS. Clinically, demyelization of the CNS results in oligodendrocyte infection with polyomaviruses. SSPE (choice E) is another slow virus disease, caused by a defective variant of the measles virus. This slowly progressive demyelization of the CNS results in death.

QUESTION 344
A 6-year-old girl has been having recurrent pyogenic bacterial infections of the sinus and respiratory tract. The latest one has been caused by N. meningitidis. The results of her diagnostic tests are shown in below figure.

TEST	RESULT
White cell count	Normal
T cell count	Normal
Production of IgM to ploysaccharides	Normal
Production of anti-DNA antibodies	Not detected
Levels of complement componets C3 and C5 to C8	Low
Levels of thyroid-stimulating hormone	Normal
Levels of immunoglobulins	Normal
Intracellular killing of microbes by neutrophils	Normal

These results are consistent with a diagnosis of which of the following?

A. chronic granulomatous disease
B. deficiency in the opsonization of microbes by phagocytes
C. Graves disease
D. systemic lupus erythematosus
E. Wiskott-Aldrich syndrome

Correct Answer: B
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
The diagnostic tests ordered by the physician are consistent with a deficiency in the C3, C5C8 components of complement. Individuals with these deficiencies have recurrent pyogenic infections, and show enhanced susceptibility to meningococcal infections. All other choices are not consistent with the laboratory findings. Chronic granulomatous disease (choice A) entails a defect in the intracellular killing of microbes by neutrophils. Graves disease (choice C) involves autoantibody production to thyroid-stimulating hormone receptors. Systemic lupus erythematosus (choice D) involves production of anti-nuclear antibodies (ANA). Wiskott-Aldrich syndrome (choice E) is associated with recurrent pyogenic infections, but is due to an inability of plasma cells to produce IgM against bacterial polysaccharides, and it occurs only in male infants.

QUESTION 345
Aprimary viral isolate from a suspected case of poliomyelitis was inoculated into cell culture, and a dramatic cytopathic effect (CPE) was noted within 24 hours. The isolate was confirmed as poliovirus by neutralization with polyvalent antibody to poliovirus types I, II, and III; however, monospecific antibody to each type failed to block CPE. This finding suggests that the isolated contained which of the following?

A. hybrid virus of type I and type II poliovirus
B. mixture of polio and another type of picornavirus mixture

C. mixture of two types of poliovirus
D. recombinant of type I and type II viruses
E. virus that shares a few antigenic determinants with poliovirus

Correct Answer: C
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
Polioviruses 1, 2, and 3 are enteroviruses that belong to the picornavirus group. Even though wild-type polioviruses have not been detected in North America for many years, both the live-attenuated and killed vaccines are currently used in pediatric vaccinations. It is fairly easy to isolate and identify poliovirus strains. In this case, poliovirus was isolated and neutralized by a polyvalent antibody against all three polio strains, prompting a presumptive diagnosis of poliomyelitis in the patient. A follow-up study using separate monovalent antibodies failed to duplicate the viral identification that was indicated by the trivalent serum product. The most logical reason for this would be that two types of polioviruses were isolated and neutralized by the polyvalent reagent but not the monovalent reagents (choice C). While work is being reported on attempts to create a recombinant virus with 1, 2, and 3 antigen markers (choice D), this has not yet become successful. Neither have any hybrid polio viruses (choice A) been reported. A mixture of poliovirus and another picornavirus (choice B) would not explain the situation described because there is little to no cross reactivity of poliovirus antisera to the other members of the picornavirus group. Choice E would not be appropriate either because no other picornavirus shares only some antigenic determinants with the polioviruses.

QUESTION 346
Which of the following correctly describes Norwalk virus?

A. contains an RNA genome with a single open reading frame
B. generally causes a severe chronic gastroenteritis with diarrhea that may persist for several weeks
C. is a major cause of severe diarrhea in infants in the developing countries
D. is an important cause of epidemic gastroenteritis in the United States
E. is diagnosed by isolation and then growth of the virus in tissue culture

Correct Answer: D
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
Many outbreaks of intestinal disease and diarrhea occur in crowded conditions like cruise ships, where hundreds of tourists become ill in a short time and the cruise must be terminated early so that treatment may be obtained and the ship sanitized. Norwalk virus belongs to the calicivirus classification and is an important cause of outbreaks of vomiting and diarrheal illness in families, communities, and institutions. It is widespread in the United States and is the most important cause of epidemic viral gastroenteritis in adults (choice D). Caliciviruses do have a single-stranded RNA genome which is positive-sense and nonsegmented. It has multiple open reading frames for translation (choice A). The gastroenteritis caused by Norwalk virus has a 2448 hour incubation, rapid onset, and a brief time course (1260

hours), not several weeks (choice B). Rotaviruses are the major cause of severe diarrhea in infants in developing and developed countries (choice C). Reverse transcriptase-- PCR is the most widely used method to diagnose Norwalk and other caliciviruses in outbreaks since the virus cannot be isolated, grown, and identified in diagnostic laboratories (choice E).

QUESTION 347
Which of the following is the best neutrophil and monocyte attractant?

A. C5a
B. HLA-A
C. HLA-B
D. J chain
E. variable region of the heavy chain of gG

Correct Answer: A
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
C5a is a component of complement. Activation of complement by endotoxin, or antigen-antibody complexes produces C5a, which is a powerful neutrophil, monocyte, eosinophil, and basophil attractant. C5a along with C3a are anaphylatoxins which mediate histamine release from mast cells leading to increased vascular permeability and vasodilation. The variable region of the heavy chain of IgG is not known as the best neutrophil or macrophage attractant (choice E). The J moiety of IgM and IgA does not possess chemotactic properties for neutrophils and macrophages (choice D). HLA-A and HLA-B are genes for the human leukocyte antigens (HLA), and they control the synthesis of class I antigens (choices B and C).

QUESTION 348
Patients with fungal pneumonias are not isolated from other patients because of which of the following?

A. These infections are caused by organisms which multiply in lymph nodes.
B. These infections are difficult to transmit from person to person.
C. These infections are eliminated quickly by antifungal drugs (ketoconazole).
D. These infections are naturally resolved in 24 hours.
E. These infections provoke an effective immune response.

Correct Answer: B
Section: Microbiology/Immunology
Explanation

Explanation/Reference:

Explanation:
In general, with the exception of some superficial infections, mycoses are not readily transmitted from person to person. Thus, patients with fungal pneumonias are not isolated, and hospital personnel are not generally required to wear masks. Fungal pneumonias are not resolved in 24 hours, they can become chronic, and they need long-term treatment with antifungal drugs (amphotericin B) due to the high percent of cases that relapse (choices C and D). Fungi that cause pneumonias are phagocytized by pulmonary macrophages and multiply in them (choice A). Most of the fungal pneumonias occur in immunosuppressed patients who do not mount an effective immune response (choice E).

QUESTION 349
German measles virus (rubella), a common cause of exanthemas in children is best described by which of the following statements?

A. incubation time is approximately 34 weeks
B. infections routinely fail to cause an immune response
C. it can be diagnosed by the presence of Koplik's spots
D. rubeola and rubella are caused by the same virus
E. specific antibody in the serum does prevent disease

Correct Answer: E
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
Rubella virus causes German measles or 3-day measles. Rubella virus is a stable RNA virus classified in the Togavirus group, but is not spread by any insect vector. The route of infection of rubella virus is the respiratory tract, with spread to the lymphatic tissue and then to the blood (viremia). Maternal viremia is followed by infection of the placenta, which leads to congenital rubella. Many organs of the fetus support the multiplication of the virus, which does not seem to destroy the cells, but reduces the rate of growth of the infected cells. Viremia develops in 79 days, not 34 weeks (choice A). Viremia lasts until the appearance of antibody on about day 1315. Rubella virus is an excellent antigen which produces an excellent, and possibly life-long, immune response (choice B). Koplik's spots (choice C) are buccal lesions that are seen in rubeola (measles) infections. Rubeola is a paramyxovirus while rubella virus, as mentioned, is a togavirus (choice D). There is an excellent live-attenuated vaccine for rubella that has been given to most children in the United States, and we have seen the number of cases drop from approximately 70,000 in 1969 to a few hundred today. Obviously, a specific antibody in the serum does prevent disease (choice E).

QUESTION 350
The tolerance of facultative anaerobic bacteria, many of which may be normal flora and opportunistic, to superoxide and hydrogen peroxide is due to which of the following?

A. absence of catalase
B. cytochrome oxidase
C. inability to form oxygen
D. presence of peroxidase

E. presence of superoxide dismutase and catalase

Correct Answer: E
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
Superoxide, which is bactericidal, is generated during electron transport and in the autoxidation of hydroquinones, leukoflavins, ferredoxins, and flavoproteins. Superoxide dismutase, however, forms oxygen and hydrogen peroxide from superoxide radicals. When catalase is present, it destroys the bactericidal hydrogen peroxide, because catalase hydrolyzes hydrogen peroxide to water and oxygen. Thus, the presence of both enzymes allows aerobes, facultative anaerobes, andaerotolerant microbes to survive when they grow in the presence of oxygen. Obligate anaerobic bacteria generally lack superoxide dismutase or catalase or both and thus cannot grow in the presence of oxygen. Oxidase is an enzyme that oxidizes a substrate by the addition of oxygen or the removal of hydrogen. It cannot oxidize the bactericidal radical superoxide (choice B). Catalase is an enzyme that converts the bactericidal substance hydrogen peroxide to water and oxygen. It has no effect on the microbiocidal action of superoxide. Bacteria that lack catalase are likely to be suppressed by hydrogen peroxide (choice A). Peroxidase is an enzyme which catalyzes the dehydrogenation of a substrate in the presence of hydrogen peroxide, which acts as hydrogen acceptor and becomes converted into two molecules of water. Thus, possession of peroxidase in a given microbe will allow it to grow in the presence of hydrogen peroxide, but not in the presence of superoxide (choice D). There are no known pathogenic bacteria that cannot form oxygen (choice C).

QUESTION 351
An injured firefighter developed a wound infection, and culture of the site indicates a gram-negative rod that is oxidase-positive and produces a bluish-green pigment. The organism was relatively resistant to antibiotics, but susceptible to ticarcillin and tobramycin. The organism is most likely to be identified as which of the following?

A. E. coli
B. Klebsiella pneumonia
C. P. mirabilis
D. P. aeruginosa
E. Serratia marcescens

Correct Answer: D
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
P. aeruginosa is a gram-negative, oxidasepositive, aerobic rod that produces a greenblue pigment called pyocyanin. This microorganism has been associated frequently with wound infections in burn patients, and it is the second leading cause of burn infections after S. aureus. P. aeruginosa tends to develop resistance to various antibiotics. However, it may respond to ticarcillin, gentamycin, tobramycin, piperacillin, or azlocillin. E. coli (choice A), K. pneumoniae (choice B), P. mirabilis (choice C), and S. marcescens (choice E) may cause urinary or pulmonary tract infections, but are not considered leading causes of burn infections. Furthermore,

these bacteria are oxidase negative and do not produce blue green pigments.

QUESTION 352
After extraction of a wisdom tooth, an 18-yearold male student was diagnosed as having subacute bacterial endocarditis. He has a congenital heart disease which has been under control. Which of the following is the most likely organism causing his infection?

A. Enterococcus faecalis
B. S. aureus
C. S. epidermidis
D. S. pneumonia
E. S. viridans

Correct Answer: E
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
The viridans streptococci include S. mitis, S. mutans, S. salivarius, S. sangus, and others. They make up a major part of oral normal flora and are alpha hemolytic. They reach the bloodstream as a result of trauma and are a principal cause of endocarditis on abnormal heart valves (choice E). They produce large amounts of polysaccharides and contribute to dental caries. S. aureus (choice B) and S. epidermidis (choice C) are usually found on the skin and may be opportunistic, but they are not as significant for endocarditis as the alpha hemolytic streptococci. E. faecalis (choice A) are usually found in the intestinal tract flora and are opportunistic if they escape that location. The major lesion for enterococci is an abscess. S. pneumonia (choice D) is primarily found in lung infections (pneumonias) and are pathogenic primarily due to their polysaccharide capsules which inhibit phagocytosis.

QUESTION 353
Persistent fever and neutropenia with persistently negative blood cultures is often caused by which of the following?

A. fungi
B. gram-negative organisms
C. gram-positive organisms
D. viral infections

Correct Answer: A
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:

Most fungi reside in nature and are essential in breaking down and recycling organic matter. About 90% of human infections by fungi can be traced to a few dozen species. Most pathogenic fungi are exogenous, their natural habitats being water, soil, and organic debris. The mycoses with the highest incidence-- candidiases and dermatophytosis--are caused by fungi that are part of the usual or normal microbial flora of humans. Most fungal growth is kept at low levels by bacteria that are more successful at using available nutrients, but fungi are efficient opportunists. Often, hosts who become infected with fungi have some serious metabolic or immune disability. Pathogenic fungi do not produce patent toxins, and the mechanisms of fungal pathogenicity are complex and multifocal, often making these infections hard to treat. The relatively low numbers of fungi in the infection and medium requirements make fungi (choice A) more difficult to isolate, identify, and relate to a medical condition. Gram-positive (choice C) and gramnegative (choice B) bacteria will usually be isolated from clinical specimens. Viral isolation (choice D) is routinely performed successfully today. The symptoms of persistent fever and neutropenia (small number of PMNs) reflect a probable infectious disease process. Failure to associate bacteria and/or viruses with an infectious disease process and clinical history might justify consideration of a fungal etiology.

QUESTION 354
Which of the following immunological assays employs separation of proteins by electrophoresis in polyacrylamide gels and subsequent transfer to nitrocellulose, followed by a reaction with antibodies?

A. complement fixation
B. enzyme-linked immunosorbent assay (ELISA)
C. immunoelectrophoresis
D. indirect fluorescent antibody test
E. Western blot

Correct Answer: E
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
In Western blots proteins are separated on the basis of molecular weight in polyacrylamide gels by electrophoresis. Then, they are transferred electrophoretically to nitrocellulose membranes and reacted with antibodies and substrate for detection. The Western blot assay is used as a confirmatory test in the determination of the HIV status of an individual. Electrophoretic transfer of proteins or antigens to nitrocellulose membranes followed by antibody reaction is not a part of complement fixation (choice A), indirect fluorescent antibody test (choice D), ELISA (choice B), or immunoelectrophoresis (choice C).

QUESTION 355
A female patient presents with swollen inguinal lymph nodes and painful lesions on the genitalia and perianal region. Which of the organisms below is the most likely causative agent for this infection?

A. Group B streptococci
B. Haemophilus aegypticus
C. H. ducreyi
D. Moraxella (Branhamella) catarrhalis

E. N. gonorrhoeae

Correct Answer: C
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
H. ducreyi (choice C) causes chancroid (soft chancre), a sexually transmitted disease. Chancroid consists of a ragged ulcer on the genetalia, with marked swelling and tenderness. The regional lymph nodes are usually enlarged and painful. Differential diagnosis must consider syphilis, HSV infection, or lymphogranuloma venereum. The organisms can usually be obtained from the lesions and often are part of a mixed infection. Scrapings from the lesion base are inoculated on to chocolate agar with X factor and vancomycin. No permanent immunity develops from chancroid infection, but the organism is treatable with ceftriaxone, TMS, or erythromycin. Group B streptococci (choice A) are usually a component of normal vaginal flora, but do not tend to be pathogenic to the host. Group B streptococci are most significant in new-born infections. H. egypticus (choice B) is most often found to be associated with conjunctivitis and Brazilian purpuric fever in children. M. catarrhailis (choice D) is a usual oral cavity organism and is considered to be an opportunist, although it has not been associated with genital infections. N. gonorrhoeae (choice E) will usually present as a mucus membrane infection with a discharge and not present as genital lesions.

QUESTION 356
A 34-year-old female patient is sneezing and has a runny nose and watery eyes every summer. Her physician is convinced that the patient is suffering from an allergy and performs some skin tests. The results of these tests are shown below:

Allergen used for testing	Response to allergen (wheal diameter in mm)
cat dander	1
house dust	4
Kentucky blue grass	13
pollen	7
fungal spores	6
solvent-only control	5

Which of the following test allergens is most likely to be inducing the patient's symptoms?

A. cat dander
B. house dust
C. Kentucky blue grass
D. mold
E. pollen

Correct Answer: C

Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
Ms Y is suffering from allergic rhinitis. The diagnosis of this allergy is made on the basis of clinical symptoms and the performance of a skin test, as well as a radioallergosorbent test (RAST). In a skin test, a battery of potential allergens is injected separately subcutaneously, and the area of the wheal and flare reaction is measured. The allergen which induces the greatest wheal and flare reaction when compared to solvent is usually the one which causes the allergy. In this case injection of Kentucky blue grass yielded the biggest wheal and flare reaction, and thus this is the allergen which caused rhinitis in the patient. Allergens such as mold (choice D), cat dander (choice A), house dust (choice B), and pollen (choice E) gave wheal and flare reactions which were either below or slightly above the skin test values of the allergen solvent. Therefore, they are not likely to be causing allergy in the patient.

QUESTION 357
Which of the following substances is most likely to prevent the attachment of the mold allergen to the sensitized mast cells in this patient?

A. complement
B. corticosteroids
C. cromolyn sodium
D. epinephrine
E. IgG anti-mold

Correct Answer: E
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
The IgG anti-mold-blocking antibody will combine with the mold allergen and will not permit the mold allergen to reach the IgE antimold on the surface of the mast cells, thus inhibiting the allergic reaction. Corticosteroids suppress inflammation, but will not prevent the attachment of the mold allergen to the sensitized mast cells by the patient (choice B). Complement is not fixed by IgE allergen complexes and plays no role in the attachment of mold allergen to sensitized mast cells (choice A). Epinephrine reverses constriction of bronchioles and bronchi, and also has no effect on the attachment of mold allergen to sensitized mast cells (choice D). Cromolyn sodium stabilizes the membrane of mast cells and thus prevents release of histamine from mast cells (choice C).

QUESTION 358
A 64-year-old alcoholic man has fever, chills, cough, and pleuritic pain. His sputum is a dark brown color, and upon cultivation on blood agar produces alpha hemolytic colonies, composed of gram- positive, optochin-positive cocci. The microbes are which of the following?

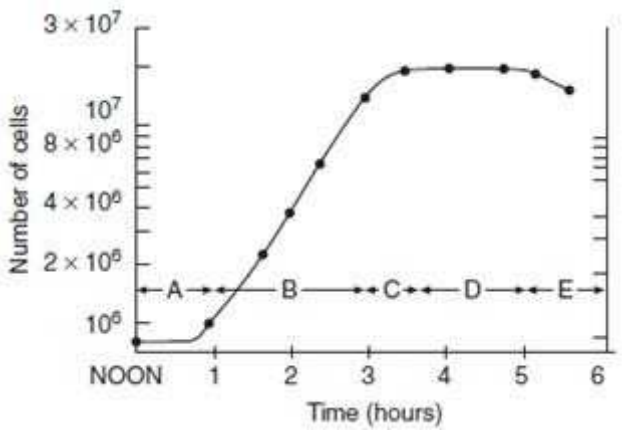
A. E. faecalis
B. N. meningitides
C. S. aureus

D. S. pneumonia
E. S. pyogenes

Correct Answer: D
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
The main symptoms of pneumonia caused by S. pneumoniae are fever, chills, and cough that produce a dark brown sputum. Alcoholism predisposes an individual to pneumonia because it reduces phagocytic activity, and promotes aspiration of microbes. In addition to S. pneumoniae (choice D), S. pyogenes (choice E), S. aureus (choice C), and N. meningitidis (choice B) can cause pneumonia. However, these other microbes do not produce alpha hemolysis and are not sensitive to optochin.

QUESTION 359
After isolating a pathogen from a patient, you monitor its growth in rich medium. According to below figure the rate of growth of the bacterial culture for which it was obtained reaches its maximum rate of growth between which of the following time periods?



A. noon and 1:00 p.m.
B. 2:00 p.m. and 3:00 p.m.
C. 3:00 p.m. and 4:00 p.m.
D. 3:00 p.m. and 5:00 p.m.
E. 4:00 p.m. and 5:00 p.m.

Correct Answer: B
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
By definition, the rate of growth of bacteria represents the change in the bacterial cell numbers over the change in time. From the choices given, the maximum rate of growth occurs between 2 p.m. and 3 p.m., where within 1 hour the number of bacteria has increased approximately threefold. Between noon and 1 p.m., 34 p.m., and 35 p.m., there is no increase in the number of cells and the rate of growth is zero.

$$\frac{2 \times 10^7 - 2 \times 10^7}{5 - 4} = 0$$

QUESTION 360
A 30-year-old previously healthy patient has all the gastrointestinal symptoms of infection with hepatitis A virus (HAV), yet all the tests for HAV-IgG and HAV-IgM are negative. Which of the following is the most likely cause of this infection?

A. hepatitis B virus
B. hepatitis C virus
C. hepatitis D virus
D. hepatitis E virus
E. rotavirus

Correct Answer: D
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
Hepatitis E virus (choice D) has been tentatively placed in the calicivirus grouping. It has been found to be the cause of another form of hepatitis and is spread by the oral-fecal route, resembling hepatitis A epidemiology. This virus, like HAV, appears to cause only acute disease and is especially dangerous to pregnant women. This cohort experienced a 20% mortality rate in an Indian outbreak in 1955. No specific diagnostic tests are currently available for HEV diagnosis. Hepatitis B (HBV--choice A) and hepatitis C (HCV-- choice B) are usually spread by means of blood and excellent diagnostic tests exist for these to diagnose specifically or rule out these agents. Hepatitis D virus (HDV--choice C) contains delta-Ag surrounded by HBV surface antigen. HDV must exist in a coinfection with HBV and may present as an acute or chronic infection. Diagnostic tests for HDV also exist. Rotaviruses (choice E) are double-stranded RNA viruses that are usually found in pediatric infections.

QUESTION 361

In a quantitative serological test, the results shown below were obtained (+ = antibody detected, 0 = no antibody detected). Which of the following courses of action should be taken?

	SERUM DILUTION					
	1:10	1:20	1:40	1:80	1:160	1:320
Test Result	+	+	+	+	+	+

A. choose another test mechanism to measure the antibody
B. perform testing on additional dilutions until an end point is reached
C. repeat the test because this pattern is impossible
D. report "negative" for antibody E) report "positive" for antibody

Correct Answer: B
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
Quantitative serological tests are being replaced by newer testing procedures, such as ELISA, which is not quantitative. Understanding how quantitative data is used diagnostically is still important clinically. For best results for interpretation, an acute and convalescent serum from thepatient should be tested at the same time. If a 4-fold (1:2 dilutions) or 100-fold (1:10 dilutions) increase in Ab titer is found, that would be a positive diagnostic result. Often, as in this case, only a single serum sample was tested. Positive results through the highest dilution of serum could represent a very high Ab level or some problem with the test procedure, giving a false-positive interpretation. The most effective way to solve this problem is to dilute the serum further and repeat the test (choice B). Once an end-point is reached, this information may confirm or deny a possible diagnosis. An alternative test mechanism (choice A) may be available, but one must remember not to use results from two test mechanisms as a direct comparison for diagnostic purposes. This pattern is not uncommon (choice C) because high antibody titers may exist in some infections (EBV, for example). Negative (choice D) or positive (choice E) would be inappropriate reports without repeating the test as described above.

QUESTION 362
A Gram-stain smear of spinal fluid from a 2- year-old child reveals short gram-negative rods. It grows on enriched chocolate agar, but does not grow on blood agar, except adjacent to a streak of staphylococci. The organism most probably is which of the following?

A. H. influenza
B. N. gonorrhoeae
C. N. meningitides
D. L. monocytogenes
E. S. pneumoniae

Correct Answer: A
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
The organisms of the genus Haemophilus are small, gram-negative, nonmotile, nonspore-forming bacilli with complex growth requirements. H. influenzae requires a heatstable factor found in blood (X factor), which can be replaced by hematin, and nicotinamide adenine dinucleotide (V factor), which can be added to the medium as a supplement, or can be supplied by other microorganisms, such as staphylococci (satellite phenomenon). N. meningitides (choice C), N. gonorrhoeae (choice D), S. pneumoniae (choice E), and L. monocytogenes (choice B) are able to synthesize hematin and nicotinamide adenine dinucleotide, and thus they will grow in culture media which do not contain these nutrients. They also do not need to rely on the production of hematin and nicotinamide adenine dinucleotide by S. aureus to grow. In contrast to H. influenzae, S. pneumonia is a gram-positive, lancet- shaped diplococcus, not a gram-negative bacterium. L. monocytogenes is a gram-positive rod.

QUESTION 363
Clinical laboratory results indicate that an AIDS patient in a county hospital in San Antonio is infected with an acid-fast bacillus. Which of the following bacteria is this organism most likely to be?

A. M. avium-intracellulare
B. M. fortuitum-chelonei
C. M. marinum
D. M. scrofulaceum
E. M. tuberculosis

Correct Answer: A
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
M. avium-intracelluaire (choice A) is often called the MAC or MAI (M. avium-intracellulaire) complex. They are ubiquitous in the environment (water, soil, food, animals). MAC organisms seldom cause disease in immunocompetent humans but are efficient opportunists in those immunocompromised, especially in AIDS patients in the United States. In fact, it is one of the most common opportunistic infections of bacterial origin in that situation. Environmental exposure can lead to MAC colonization of either the respiratory or GI tract. A transient bacteremia is usually followed by tissue invasion. Any organ may be affected. A wide variety of clinical presentations may occur, but patients often present with nonspecific symptoms of fever, night sweats, abdominal pain, and diarrhea and weight loss. Diagnosis is made by culturing the organism. Treatment may involve multiple drugs and last from 6 months to 1 year or even for life. M. fortuitum-cheloni (choice B) are soil/water saprophytes and may cause superficial or systemic disease only rarely. M. marinum (choice C) occurs in water and may cause skin lesions in humans. Infections are relatively rare.M. scrofulaceum (choice D) is also found in water and may be a rare saprophyte in adults with chronic lung disease. M. tuberculosis (choice E) causes tuberculosis in humans and is a very important human pathogen. Host to host transmission is the usual method observed.

QUESTION 364

Within hours after being bitten by a cat trapped in a flood drain, a member of the rescue team develops redness, swelling, and intense pain at the site of the bite. Laboratory results indicate the presence of mixed flora in the wound, including a gram-negative rod that is frequently associated with cat and dog bites and that often leads to complications such as osteomyelitis if untreated. Which of the following is most likely to be this organism?

A. B. canis
B. C. coli
C. Francisella tularensis
D. Pasteurella multocida
E. P. aeruginosa

Correct Answer: D
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
Pasteurella species are primarily animal pathogens, but they can produce a range of human diseases. All yersiniae and franciseliae were formerly classified under this genus. P. multocida (choice D) occurs worldwide in the respiratory and GI tracts of many domestic and wild animals. It is the most common organism in humans inflicted by bites from cats and dogs. It may produce human infections in many systems and may, at times, even be part of the normal/usual human flora. Ahistory of animal bite, pain and pus drainage at the bite site, gram-negative bipolar rods, and culture of the organism would confirm the diagnosis. B. canis (choice A) may cause mild reticuloendothelial disease in humans. F. tularensis (choice C) can be transmitted by direct contact with infected animal tissues or by inhalation or ingestion, seldom if ever by bites. C. coli (choice B), along with C. jejuni, are common human pathogens, causing mainly enteric infections. P. aeruginosa (choice E) is widely distributed in nature and in moist environments in hospitals. It can cause opportunistic diseases in immunocompromised humans. Such infections may present with bluegreen pus and are difficult to treat with antimicrobials.

QUESTION 365
Which of the following immunoglobulins is responsible for passing the placental barrier and attacking the Rh+ fetal red blood cells in hemolytic disease of the newborn (erythroblastosis fetalis)?

A. IgA
B. IgD
C. IgE
D. IgG
E. IgM

Correct Answer: D
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
There are five known classes of immunoglobulins: IgG, IgA, IgM, IgD, and IgE. IgG is the major immunoglobulin that is found in human serum and the only one that has been shown to pass the placental barrier in humans. IgM possesses higher agglutinating and complement-fixing capacity than IgG. IgM has a molecular weight of 900,000. Carbohydrates constitute 711% of the total weight of IgM (choice E). IgD constitutes a minor portion of serum immunoglobulins (1%). It contains higher amounts of carbohydrate (13%) than the other immunoglobulins, but it is an important B-cell receptor. No other biological functions have been described for IgD (choice B). IgE is the immunoglobulin that has been associated with anaphylactic hypersensitivity. IgE has a molecular weight of 190,000 200,000, contains 1112% carbohydrate, and constitutes 0.002% of the total serum immunoglobulin (choice C). IgA is the major immunoglobulin of extracellular secretions. It has a molecular weight of 160,000440,000, has modest agglutinating capacity, and its carbohydrate content is two to three times higher (7.5%) than that of IgG (choice A).

QUESTION 366
A 27-year-old man was treated with penicillin for gonorrhea. Thirty-five days later he was reinfected with the same germ, and his physician administered an intramuscular dose of penicillin. Two minutes following the injection of penicillin, the patient experienced hypotension and shock and became unconscious. This reaction was most likely mediated by which of the following?

A. activation of the alternate complement pathway
B. activation of the classical complement
C. IgD
D. IgE
E. IgG

Correct Answer: D
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
Anaphylaxis triggered by penicillin is an immediate hypersensitivity reaction, which is typically mediated by IgE antibodies. IgE antibodies bind to specific Fc receptors on the surface of mast cells and basophils. Upon cross-linking of the IgE antibodies with their specific antigen (penicillin in this case), mast cells and basophils release histamine within minutes along with other pharmacologically active shock mediators which produce the characteristic symptoms of anaphylaxis. Activation of either the classical (choice B) or the alternate complement pathway (choice A) does not play any meaningful role in anaphylaxis. IgD (choice C) and IgG (choice E) are not involved in anaphylactic reactions.

QUESTION 367
A 78-year-old patient with an episode of acute urinary retention was catheterized. Three days later, he developed fever and suprapubic pain. Culture of the urine revealed a thin film of bacterial growth over the entire blood agar plate, and the urease test was positive. Which of the following is the most likely organism to cause this infection?

A. E. faecalis
B. E. coli

C. H. pylori
D. Morganella morganii
E. P. mirabilis

Correct Answer: E
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
Proteus species (choice E) produce disease in humans only when the bacteria leave the intestinal tract. P. mirabilis routinely causes urinary tract infections and produces urease. In such urinary tract infections, the urine becomes alkaline, promoting stone production. The organism is rapidly mobile, resulting in swarming on agar plates and may be a virulence factor in the urinary tract invasion. Proteus species are resistant to many antimicrobials. E. coli (choice B) is urease negative, and while motile, does not swarm on agar. H. pylori (choice C) is motile and a strong producer of urease, which is used to modify gastric mucus for more efficient growth in the intestinal tract. Gastritis and peptic ulcers are produced by H. pylori. Morganella morganii (choice D) is similar to proteus but observed only in occasional infections. E. faecalis (choice B) are gram-positive cocci which are urease negative and form colonies on blood agar, not swarming.

QUESTION 368
A similar virus was isolated from several students in a day-care school that experienced a respiratory disease outbreak. This virus passes through a 50 nm filter, grows best in human diploid fibroblasts at 33℃, is not inactivated by chloroform, is inactivated at pH 3, and is inhibited by compounds that interact with the interior of grooves on the viral surface that attach to cell receptor molecules. Which of the following is the most likely virus based upon its identifying characteristics?

A. coronaviruses
B. Influenza virus B
C. respiratory syncytial virus
D. rhinovirus
E. rubella virus

Correct Answer: D
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
Rhinoviruses (choice D) are common cold viruses that belong to the picornavirus group. They are small (2830 nanometers), have a positive-sense linear RNA genome, and no lipid envelope. The viral receptor is located in a groove or canyon in the capsid coat where the cellular receptor (ICAM-1) attaches in the initial cell infection process. The incubation period is brief (12 days), allowing many infections to occur in a crowded or closed living situation. Coronaviruses (choice A) are also common cold viruses but larger than 50 nm and has a lipid envelope. Influenza viruses (choice B) are also larger than 50 nm and possess lipid envelopes. RSV (choice C) and rubella virus (choice E) are similar, being larger than 50 nm with lipid envelopes.

QUESTION 369
Sputum from a patient with a respiratory infection reveals bacteria that resist engulfment by phagocytic WBCs. Which of the following factors is most likely responsible for this virulence?

A. A capsule
B. fimbriae
C. flagella
D. lipid A
E. peptidoglycan

Correct Answer: A
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
Capsules (choice A) are usually made of polysaccharides and allow bacteria to resist phagocytosis by PMNs and macrophages. Since the capsule contributes to the invasiveness of pathogenic bacteria, it is considered a virulence factor. If the host produces an antibody against the capsule materials, phagocytosis and destruction of the organism can occur. Fimbriae (choice B) are also called pili and attach to cell surfaces to promote microbial colonization. While some bacteria (N. gonorrhoeae, for instance) produce pili and are able to resist phagocytosis if firmly attached, fewer kinds of bacteria produce pili than those capable of producing capsules. Flagella (choice C) are organelles of locomotion and do not resist phagocytosis. Lipid A(choice D) is a component part of endotoxin from gram- negative cell walls. It is considered to be the toxic component of endotoxin, capable of causing inflammation, but does not resist phagocytosis. Peptidoglycan (choice E) is part of gram-positive cell walls. Peptidoglycans do not resist phagocytosis directly but do contain techoic acid residues that allow bacteria to adhere to cells.

QUESTION 370
A 75-year-old lady is slowly developing a chronic suppurative cervicofacial lesion, thought to be actinomycosis. Which of the following is most likely to promote the progress of this infection?

A. high levels of oxygen in tissues
B. presence of a foreign body at the site of infection
C. production of exotoxin by A. israelii
D. production of leukocidin by A. israelii
E. production of pili by A. israelii

Correct Answer: B
Section: Microbiology/Immunology
Explanation

Explanation/Reference:

Explanation:
A. israelii is an opportunistic microorganism that does not produce any known virulence factor. It seems that its pathogenesis is related to the ability of this organism to survive the host's inflammatory responses. Devitalized tissues, presence of foreign bodies, broken mucous membranes, and immunosuppression promote development of actinomycosis. A. israelii is an anaerobic organism. Thus high levels of oxygen will kill this microbe (choice A). This bacterium does not produce leukocidin (choice D), exotoxin (choice C), or pili (choice E).

QUESTION 371
An X-linked recessive B-cell immune deficiency associated with a defect in the tyrosine kinase gene and low levels of all antibody classes is most likely to present with repeated infections involving which of the following?

A. extracellular bacteria
B. fungi
C. intracellular bacteria
D. P. carinii
E. viruses

Correct Answer: A
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
Individuals who have been diagnosed as Xlinked agammaglobulinemic lack B lymphocytes and are not able to produce immunoglobulins. The lack of immunoglobulins in X-linked agammaglobulinemia renders individuals susceptible to a succession of infectious diseases caused by extracellular bacteria. These infections may be partially controlled by the injection of specific gamma globulin as a supportive therapy. Xlinked agammaglobulinemic patients have T cells that are the key players in cell- mediated immunity associated with graft rejection, intracellular parasites (choice C), viruses (choice E), and fungi (choice B). P. carinii (choice D) is now considered a fungus, causing infections in immunocompromised patients, such as those with AIDS.

QUESTION 372
Gene therapy has taken an approach of expressing TNF in tumor-infiltrating lymphocytes (TIL). It is hoped that this approach will induce which of the following events?

A. allow the TIL to return to the tumor and produce locally high levels of TNF
B. generate high serum levels of endotoxin
C. lyse tumor cells due to retrovirus infection
D. stimulate natural killer (NK) cell activity
E. stimulate T-cell proliferation

Correct Answer: A

Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
TNF is cytotoxic to certain tumor cells. Recent experiments in gene therapy have taken the approach of expressing TNF in TIL, with the hope of allowing the TIL to return to the tumor and produce a high concentration of TNF and kill the tumor cells. TNF is a mediator of endotoxin- induced shock and is involved in inflammation, but does not generate high levels of endotoxin (choice B). There is no evidence to support that TNF stimulates T-cell proliferation (choice E). TNF is cytotoxic to certain tumor cells, but it does not lyse tumor cells by retroviral participation (choice C). NK cells can destroy tumor cells; however, they cannot be stimulated by TNF (choice D).

QUESTION 373
A 2-year-old boy who has not been vaccinated against any germ is experiencing severe spasms in the muscles of the jaw and face. These spasms do not allow the child to open his mouth. Laboratory tests established that a bacterial toxin was responsible for this boy's symptoms. The toxin involved was most likely produced by which of the following organisms?

A. C. botulinum
B. C. perfringens
C. C. tetani
D. C. diphtheria
E. V. cholerae

Correct Answer: C
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
Tetanus toxin produced by C. tetani is a protease that often first affects the masseter muscles. Patients so affected cannot open their mouths and have what is called trismus. Trismus provides an explanation for the term lockjaw used to describe tetanus. Cholera toxin (choice E--V. cholerae) causes fluid and electrolyte loss that leads to severe diarrhea. The clostridial alpha toxin (choice B--C. perfringens) kills cells and produces necrosis. Diphtheria toxin (choice D--C. diphtheriae) is an inhibitor of protein synthesis affecting heart, kidney, and other cells. Protein synthesis is inhibited because diphtheria exotoxin catalyzes the polyADP-ribosylation of eukaryotic elongation factor 2 (eEF2). Botulinum toxin (choice A) cleaves the proteins involved in the release of acetylcholine. This leads to aralysis of ocular, pharyngeal, and respiratory muscles.

QUESTION 374
Acollege freshman exhibits symptoms of fever, malaise, sore throat, and fatigue. She also has enlarged lymph nodes and spleen and large, atypical T-lymphocytes. Which of the following tests can be used to confirm which virus is the etiologic agent?

A. antibody that reacts with Epstein-Barr virus (EBV)-associated nuclear antigen

B. antibody to hemagglutinin
C. antibody to neuraminidase (NA)
D. heterophile antibody that reacts with antigens on sheep erythrocytes
E. nucleic acid hybridization assays for the presence of Epstein-Barr viral nucleic acid

Correct Answer: E
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
Infectious mononucleosis is caused by EBV, which is a member of the herpesviruses. Nucleic acid hybridization assays for EBV DNAare the most sensitive means of diagnosing infectious mononucleosis. Hemagglutinins (choice B) and NAs (choice C) are associated with orthomyxoviruses and paramyxoviruses. The majority of infectious mononucleosis patients develop what is known as an heterophile antibody, antibodies that cross-react with unrelated antigens, such as those found on sheep and horse erythrocytes. The heterophile antibody test (choice D) is used for the diagnosis of infectious mononucleosis, but since it is not a very specific test, it is not as good as the nucleic acid hybridization assays for the presence of Epstein-Barr viral nucleic acid. Important antigens that also may be used, but which are less sensitive for diagnostic purposes, include the viral capsid protein (VCA), the early proteins (EA), and the EBV-associated nuclear antigen (EBNA). Infectious mononucleosis patients develop antibody titers exceeding 1:320 and 1:20 against VCA and EA, respectively, during the acute phase of infectious mononucleosis. Antibodies to EBNA develop 12 months after acute infection (choice A).

QUESTION 375
Ahemagglutination (HA) assay was performed with influenza virus. Afixed number of chicken red blood cells were mixed with increasing dilutions of the influenza virus. The results of the assay are shown in below figure. Which of the following represents the HA titer of the virus?

A. 20
B. 40
C. 80
D. 160
E. 320

Correct Answer: C
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
The ability of certain viruses, such as influenza, mumps, and parainfluenza viruses, to agglutinate red blood cells is used to diagnose these viruses. In general, chicken or human type O red blood cells are employed for the identification of influenza and other viruses. Red blood cells have receptors for the surface component of the influenza virus called hemagglutinin. This hemagglutinin is a glycoprotein. In an HA assay, a fixed number of red blood cells is mixed with increasing dilutions of the influenza virus. Following incubation at 4℃ for 2 hours, the tubes contai ning the red blood cells and the virus are examined for HA. Cells agglutinated by the virus form a lattice that covers the entire bottom of the test tube (virus dilutions 1:20; 1:40; 1:80). The HA titer of the virus is the highest dilution of virus that forms a lattice. In this case, the HA titer is 1:80. Unagglutinated cells form a dark bottom (virus dilutions 1:160; 1:320) (choices D and E).

QUESTION 376
HIV isolated from the same patient over time may differ antigenically. HIV also differs from the viruses found in the general class of RNA tumor viruses. Which of the following best explains how HIV differs from most other RNA tumor viruses?

A. HIV contains the gag gene
B. HIV contains the pol gene
C. HIV contains two copies of singlestranded RNA in its virion
D. HIV does not require T4 receptor protein for adsorption to host cells
E. HIV lyses the host cells

Correct Answer: E
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
An important difference between the AIDS (HIV) virus and the RNA tumor viruses is that HIV lyses the host cells, while RNA tumor viruses transform the cells they invade, butthey lack cytolytic activity. The tropism of the HIV for T4 lymphocytes depends on the presence of the T4 protein on the surface of the lymphocytes. This protein serves as the receptor for the adsorption of the HIV to T4 lymphocytes. The HIV is a member of the retroviruses (choice D). The genomic RNA molecule of HIV contains the gag, pol, and env genes. Thus, the HIV does not differ from RNA tumor retroviruses (choices A and B). HIV contains one copy, not two, of single-stranded RNA in its virion (choice C).

QUESTION 377
A 24-year-old construction worker who had four injections of the DPT (diphtheria, pertussis, and tetanus) vaccine in his first year of life and boosters at ages 5 and 19 received a deep laceration while excavating a building's foundation. Which of the following is the preferred treatment?

A. equine tetanus immune globulin, because it will passively immunize him
B. human tetanus immune globulin, because it will stimulate his anamnestic response
C. penicillin, because it will kill the organism
D. streptomycin, because it will kill the organism

E. tetanus toxoid, because it will stimulate his anamnestic response

Correct Answer: E
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
Since there are memory lymphocytes primed by a previous tetanus toxoid injection, booster immunization with tetanus toxoid will lead to rapid production of adequate levels of protective antibody. This is the routine procedure followed by physicians for trauma patients, who have been accinated against tetanus and received booster immunization within the last 57 years. The antibody titer to tetanus toxoid remains at protective levels for 510 years. Aminoglycosides such as streptomycin (choice D) or penicillin (choice C) will not be effective against the spores or vegetative cells of C. tetani. Human tetanus immune globulin will only provide antibodies to tetanus exotoxin for a short time and cannot induce an anamnestic response because an injection of tetanus exotoxin or toxoid is required (choice B). Individuals who have been vaccinated against tetanus require injections of the tetanus toxoid to induce rapid production of adequate levels of protective antibody. Treatment with equine tetanus immunoglobulin, which will only provide antitetanus antibody for a short time, is not the preferred method of treatment for this patient (choice A).

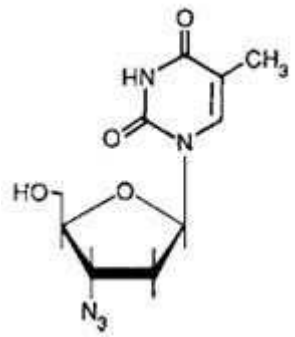
QUESTION 378
A Boy Scout troop camped for 1week in the woods in the New England area. After arriving home, two experienced an insect bite lesion that was characterized by a clear center surrounded by a flat reddened area that expanded. They also had fever, chills, fatigue, and headache. Which disease listed below was diagnosed?

A. epidemic typhus
B. lyme disease
C. Q fever
D. rickettsial pox
E. trench feve

Correct Answer: B
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
This patient's symptoms point to a diagnosis of Lyme disease, caused by B. burgdorferi, and transmitted to humans by ticks that harbor this organism. The initial symptoms of Lyme disease are fever, chills, fatigue, and headache, but the pathognomonic feature is a spreading, circular rash with a clear center. The rash begins 318 days after the tick bite and is called erythema chronicum migrans. Q fever (choice C), epidemic typhus (choice A), rickettsial pox (choice D), and trench fever (choice E) do not produce erythema chronicum migrans.

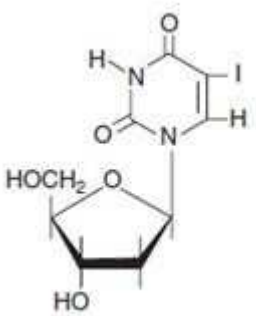
QUESTION 379
Ayoung street person was treated with the drug the structure of which is shown in below figure. Which of the following correctly identifies the drug?



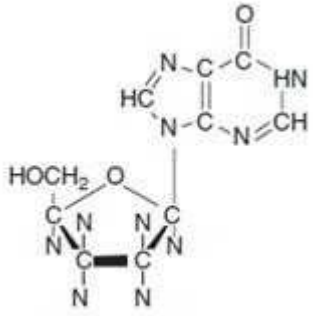
A. acyclovir, which inhibits the herpesvirus- encoded DNA polymerase
B. azidothymidine (AZT), which inhibits the AIDS virus reverse transcriptase
C. dideoxyinosine, which inhibits poliovirus replication
D. enviroxine, which inhibits rhinoviruses
E. idoxuridine, which inhibits herpesvirus thymidine kinase

Correct Answer: B
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
The antiviral drug currently used against the immunodeficiency virus is AZT, or 3-azido-3- deoxythymidine (azidothymidine). Its structure is shown in below figure.
The structures of related compounds idoxuridine (choice E) and dideoxyinosine (choice C) are shown below in below figure.
Acyclovir (choice A) and enviroxine,



Idoxuridine



Dideoxyinosine (ddI)

(choice D) differ chemically from the structure depicted in below figure

QUESTION 380
Agrandmother undergoing chemotherapy for cancer in a hospital was exposed to a grandchild with chickenpox. In order to prevent a clinical complication of varicella or disseminated zoster in the grandmother, which of the materials listed below should be used as an appropriate medical intervention?

A. acyclovir
B. indinavir
C. killed varicella-zoster virus (VZV) vaccine
D. live attenuated VZV vaccine
E. subunit VZV vaccine

Correct Answer: A
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
Prevention of varicella and disseminated zoster rests on the administration of acyclovir. Killed varicella-zoster virus (VZV) vaccine has not been shown to be effective. Furthermore, if the immunological system has been compromised the immune responses will be very weak and of questionable value (choice C). Live attenuated VZV vaccines cannot be given to immunocompromised individuals because vaccination can be lethal (choice D). Subunit VZV vaccines are not available, and will be of little value to persons with suppressed immunological responses (choice E). Indinavir is a protease inhibitor used for the treatment of AIDS, not for varicella or zoster (choice B).

QUESTION 381
A young child developed staphylococcal scalded syndrome. Which one of the following toxins is most likely responsible for this syndrome?

A. alpha toxin
B. erythrogenic toxin
C. exfoliative toxin
D. staphylococcal enterotoxins A through F
E. toxic shock syndrome toxin (TSST)

Correct Answer: C
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
Exfoliation toxin is produced by certain strains of S. aureus belonging to phage group II. This exotoxin divides the epidermis between the stratum granulosum and the stratum spinosum. The end result of exfoliation action is the exfoliation of the skin, known as the staphylococcal scalded skin syndrome. The TSST (choice E) causes multisystem involvement with shock which can be lethal. TSST is a super antigen that releases large concentrations of IL-1, IL-2, and TNF. Erythrogenic toxin (choice B) is produced by S. pyogenes and is associated with scarlet fever. Alpha toxin (choice A) is produced by S. aureus and causes necrosis and hemolysis of blood cells. Staphylococcal enterotoxins A through F (choice D) are responsible for food poisoning.

QUESTION 382
A 3-year-old child presents at the physician's office with symptoms of coryza, conjunctivitis, low- grade fever, and Koplik's spots. The causative agent of this disease belongs to which group of viruses?

A. adenovirus
B. herpesvirus
C. orthomyxovirus
D. paramyxovirus
E. picornavirus

Correct Answer: D
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
Measles or rubeola belongs to the paramyxovirus group (choice D). Measles is an acute, highly infectious disease characterized by fever, respiratory symptoms, and a maculopapular rash. Complications are common and serious. Humans are the only natural host for measles virus, which is spread by respiratory secretions. The virus grows first in the respiratory tract and then to the local lymphatics. Koplik's spots can be observed in the buccal mucosa. The virus replicates in the RE system and is then spread to the skin and other epithelial surfaces. The incubation period can be up to 3 weeks and the rash can last up to 2 weeks (hard

measles). The rash appears to be a T-cell interaction with virus-infected cells. The main complication involves the CNS and lungs. Arare complication is SSPE. An excellent live-attenuated virus vaccine has been widely used and has decreased measles presence in the population greatly. Immunity (natural or artificially acquired) is lifelong. Adenovirus (choice A) is most often seen as respiratory infections, although significant eye and enteric diseases are caused by different strains of adenovirus. Herpesvirus (choice B) produces crops of vesicular lesions, not a maculopapular rash. Othromyxovirus (choice C) is influenza, which has no rash presentations. Picornaviruses (choice E) consist of polioviruses, coxsackieviruses and ECHO viruses. Koplik's spots do not appear in these infections although macular rashes may occasionally be observed.

QUESTION 383
A 25-year-old woman develops fever, sore throat, headache, and generalized lymphadenopathy, a macular non-pruritic rash over the trunk and limbs, flat papular lesions on her inner thighs. Initial serological tests are positive for Treponema species. Which of the following represents the diagnosis for this condition?

A. condylomata lata
B. primary syphilis
C. secondary syphilis
D. tertiary syphilis
E. yaws

Correct Answer: C
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
Natural infections with T. pallidum are limited to the human host, usually by sexual contact. The infectious lesion is on the skin or mucus membranes of the genitalia. Spirochetes multiply locally at the site of entry and spread to the local lymph nodes and the blood stream. Several weeks later, a papule develops at the site of infection and develops into a lesion (hard chancre). This primary lesion (choice B) "heals" spontaneously, but "secondary" lesions appear 23 months later. These include a red maculopapular rash and moist, pale papules (condylomas) in the genital region, axillas and mouth (choice C). Syphilitic meningitis, chorioretinitis, hepatitis, nephritis, or periostitis may occur. Both primary and secondary lesions are filled with infectious spirochetes. The infection goes subclinical. About 30% of cases cure spontaneously, while another 30% remain latent. In the rest, the disease progresses to the tertiary (choice D) stage characterized by the development of granulatomatous lesions (gumma) in the skin, bones, and liver. Degenerative changes can occur in the CNS or cardiovascular system. Spirochetes are rare at this stage. T. pallidum cannot be cultured, and the disease is usually confirmed by serological tests. Penicillin remains the treatment of choice, but prolonged follow-up is essential. Yaws (choice E) is a disease that is usually seen as ulcerating papules on the skin of arms or legs and is caused by a variant of T. pallidum. Direct contact is the usual transmission mechanism. Condylomata lata (choice A) refer to eroded papules that fuse together and are highly infectious during secondary syphilis.

QUESTION 384
A 58-year-old nurse has a herpetic infection that requires administration of acyclovir. Which one of the following is the known mechanism of action of acyclovir?

A. degradation of viral RNA
B. inhibition of reactivation of virus in trigeminal root ganglia

C. inhibition of viral RNA synthesis
D. killing of actively dividing cells in which virus replicates
E. termination of DNA replication of herpes virus

Correct Answer: E
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
Acyclovir is a guanosine analogue which inhibits viral DNA synthesis. It is activated in cells by the virus-encoded thymidine kinase, which phosphorylates this drug. Only viruses that produce thymidine kinase, such as herpes simplex 1 and 2 or the varicella-zoster virus are susceptible to acyclovir. This antiviral agent has not been shown to inhibit reactivation of herpes virus in trigeminal ganglia (choice B), to kill actively dividing cells in which virus replicates (choice D), to degrade (choice A), or to inhibit viral RNA synthesis (choice C).

QUESTION 385
Asuburban housewife was pricked by a thorn while pruning her roses. Four days later, a pustule that changed to an ulcer developed in the lesion area. Then three nodules formed along the local lymphatic drainage. The most likely agent is which of the following?

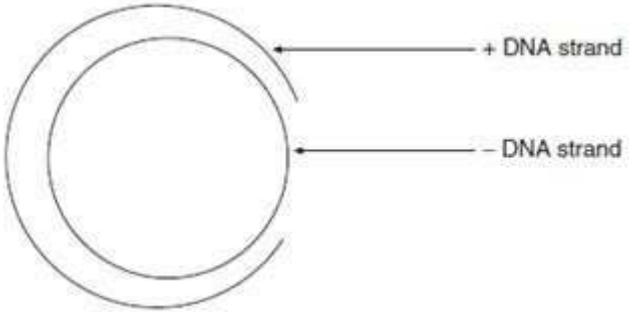
A. A. fumigates
B. C. albicans
C. Cryptococcus neoformans
D. Sporothrix schenckii
E. Trichophyton rubrum

Correct Answer: D
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
S. schenckii is found on thorns, and it is introduced into the skin of extremities through trauma. A regional lesion begins as a pustule, abscess, or ulcer, and then nodules and abscesses are formed along the lymphatics. The history and the symptoms described in this patient are consonant with a diagnosis of sporotrichosis. A. fumigatus (choice A) and C. albicans (choice B) are associated with deep opportunistic infections in immunocompromised patients such as AIDS patients. Aspergillosis is basically a pulmonary infection. Candidiasis can be associated with pathological conditions of the mucous membranes of the respiratory, genital, and gastrointestinal tract, where it is found as a normal inhabitant. C. neoformans (choice C) is the cause of meningitis. T. rubrum (choice E) is the cause of dermatophytosis ringworm of skin, scalp, and especially nails. The nails thicken and are discolored.

QUESTION 386
A 53-year-old alcoholic man had been experiencing acute episodes of nausea and eventually jaundice. Avirus was detected from him, which had a circular

molecule of DNA having the structure diagrammed in below figure. Which virus listed below has this type of genome?

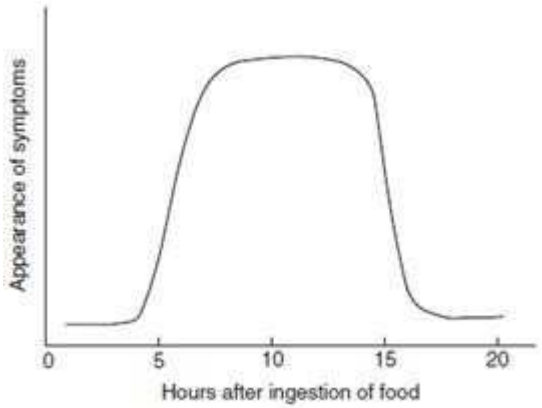


A. EBV
B. hepatitis A virus
C. hepatitis B virus
D. JC virus
E. papillomavirus

Correct Answer: C
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
The genome of hepatitis B virus is composed of a circular, double-stranded DNA. It has a negative strand of 3200 nucleotides and another positive, incomplete strand of 17002600 nucleotides. Papilloma (choice E) and polyomaviruses belong to the family of Papoviridae, which lacks envelopes and have a double-stranded, circular DNA genome. Both strands are complete and thus differ from the genome of hepatitis B virus that has one incomplete positive strand. Hepatitis Avirus (choice B), the cause of infectious hepatitis, has a linear single-stranded RNA genome, and as such it is a member of the enteroviruses. EBV (choice A) is a member of the herpesviruses and as such has a double-stranded, linear DNA genome. EBV has been associated with infectious mononucleosis, Burkitt lymphoma, and nasopharyngeal carcinoma. JC virus (choice D) is a member of the polyomaviruses.

QUESTION 387
Judging from the graph in below figure



which microorganism is likely to be the causative agent of food poisoning characterized by diarrhea and severe vomiting related to heat-stable enterotoxins?

A. C. jejuni
B. Salmonella typhimurium
C. S. aureus
D. Yersinia enterocolitica
E. V. parahaemolyticus

Correct Answer: C
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
The short incubation of 4 hours indicates staphylococcal food poisoning. This is a situation arising from the ingestion of preformed staphylococcal enterotoxin, which induces symptoms within 16 hours following consumption of contaminated food, including diarrhea, abdominal cramps, and severe vomiting. These symptoms last for 612 hours, and complete recovery usually occurs in less than 1 day. The incubation periods for S. typhimurium (choice B), V. parahaemolyticus (choice D),Y. enterocolitica (choice E), and C. jejuni (choice A) are 812, 2496, 2448, and 72168 hours, respectively. These longer incubation periods in comparison to the incubation period of staphylococcal food intoxication are due to the need for these bacteria to invade the human intestinal tract, and then multiply and form the toxins responsible for the infective form of food poisoning.

QUESTION 388
Ajudge has a fungal infection known as "Tinea cruris." Which one of the following statements concerning this infection is accurate?

A. It cannot be transmitted from person to person.

B. It involves a fungus that produces aflatoxins.
C. It is associated with athlete's foot.
D. It is caused by a fungus that forms tuberculate macroconidia.
E. It occurs primarily in immunocompromised individuals.

Correct Answer: C
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
Tinea cruris or as commonly known "Jock itch" is typically found in young men, especially in macerated or occluded areas. It is also associated with tinea pedis (athlete's foot) and the causative agent (T. rubrum or T. mentagrophytes) may be easily seen in skin scrappings. Tinea cruris occurs in ealthy and immunosuppressed persons (choice E). Histoplasma capsulatum, the causative agent of histoplamosis, forms septate hyphae with tuberculate macroconidia (choice D). In contrast to other fungal infections, tinea cruris is transmitted from person to person (choice A). Aspergillus flavus, not T. rubrum or T. mentagrophytes, produces aflatoxins, which can cause liver damage (choice B).

QUESTION 389
Poliovirus type 2 has been isolated from the stool of a 55-year-old patient who has experienced malaise, fever, nausea, and vomiting. An infant grandchild was vaccinated about 3 weeks prior to onset of the disease. What should the laboratory do to determine whether the isolated virus is related to the vaccine strain or a wild-type virus?

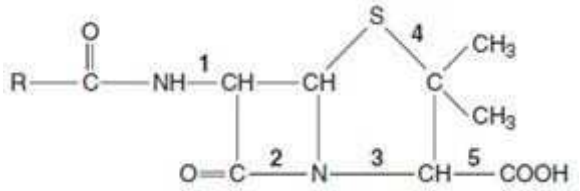
A. determine the cytopathic effects of the virus
B. do neutralization studies using the infant's serum
C. do oligonucleotide mapping of the wildtype and vaccine strains
D. inoculate the virus into mice to determine whether it kills them
E. stain the virus with fluorescent antibody

Correct Answer: C
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
To determine whether the poliovirus is a wild-type virus or if it is related to that used for vaccination, it will be necessary to prepare oligonucleotide maps of the isolated virus and compare them to those of the wild-type and vaccine strains. Many viruses may kill mice; thus, one cannot determine whether poliovirus strains are related or unrelated by mouse lethality studies (choice D). Cytopathology cannot be used for definitive diagnosis of poliovirus strains or other types of viruses (choice A). Viral neutralization assays using the grandchild's serum will only indicate whether the grandchild has been exposed to and vaccinated for the polioviruses in question, but will not establish whether the poliovirus isolated from the stool of the grandfather is related to the poliovirus used to vaccinate his grandchild (choice B). Staining of the virus with fluorescent antibody may detect the presence of poliovirus, but will not establish whether the poliovirus is a wild-type

virus or if it is related to that used for vaccination (choice E).

QUESTION 390
Two days following surgery to repair a defective valve, a patient developed an acute infection caused by a penicillin-resistant strain of S. aureus. below figure shows the penicillin molecule. Which numbered bond in the structure is the site of action of penicillinase?



A. 1
B. 2
C. 3
D. 4
E. 5

Correct Answer: B
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
An important part of the penicillin molecule is the beta-lactam group. This group is composed of two carbon and two hydrogen atoms at the top of the group. The bottom part of the group contains one carbon, which is linked to one nitrogen atom and one oxygen atom. Penicillinase breaks the bond between the bottom carbon and nitrogen atom, and destroys the antibacterial activity of penicillin, along with that of cephalosporin, which also possesses a beta-lactam group.

QUESTION 391
A 37-year-old male patient presents with a necrotizing skin lesion on the trunk of the body subsequently identified as Blastomyces dermatiditis. Which is the most likely route of entry for this organism?

A. contaminated water
B. illicit drug use
C. lung inhalation
D. skin prick
E. spoiled food

Correct Answer: C
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
B. dermatiditis is a dimorphic fungus, producing hyphae and conidia at room temperature but large, singly budding yeast cells at 37℃. Blastomycosis is a chronic infection with granulomatous and suppurative lesions that is initiated in the lungs. Inhalation (choice C), therefore, would be the mechanism of entry for this organism. It can disseminate to any organ, but the skin and bones appear to be the most common site. Interestingly, while B. dermatiditis is endemic for humans and dogs in the United States, it is not directly transmitted from either of these sources. It is thought to be derived from the environment, perhaps with some factor associated with rivers. It can be treated with amphoteracin B. No reports of transmission have been reported from consuming contaminated water (choice A), drug use (choice B), skin penetration (choice D), or ingestion of food (choice E), spoiled or otherwise.

QUESTION 392
A 25-year-old male patient comes to your office experiencing inability to swallow and speech difficulty. The patient was in perfect health prior to the consumption of home-canned green beans. Which of the following is the most likely method of treatment?

A. administration of staphylococcal enterotoxin antiserum
B. administration of trivalent botulinum antitoxin
C. immunization with S. aureus enterotoxin toxoid
D. penicillin administration
E. placement of the patient in a hyperbaric oxygen chamber

Correct Answer: B
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
The patient described in this question is showing the typical symptoms of botulism, which is commonly caused by types A, B, or E C. botulinum toxin. Therefore, early administration of potent botulinum antitoxin-containing antibodies to toxins A, B, and E constitutes the most appropriate type of treatment. Administration of staphylococcal enterotoxin antiserum could have been helpful if the atient was suffering from staphylococcal food poisoning, but he is not (choice A). Immunization with staphylococcal enterotoxin toxoid (choice C), administration of penicillin (choice A), or placing this patient in a hyperbaric chamber (choice E) are all useless.

QUESTION 393
Antibiotic therapy is a critical step in the proper management of many patients infected with various types of bacteria. Infection with which microorganism listed below would not benefit from even prompt antimicrobial treatment?

A. B. anthracis
B. C. botulinum

C. C. difficile
D. C. perfringens
E. C. tetani

Correct Answer: B
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
Botulism is worldwide in distribution and is caused by C. botulinum (choice B). C. botulinum is an anerobic, spore-producing grampositive organism. During the growth of the vegetative form of the organism, toxins (types AG) are liberated into the environment, especially when the bacteria undergo autolysis. Illness in humans is most often caused by ingestion of foods contaminated with the toxin. Botulism toxin is absorbed from the gut and binds to receptors of presynaptic membranes of motor neurons of the peripheral nervous system and cranial nerves. This inhibits the release of acetylcholine, producing a flaccid paralysis. Use of antibiotics would be inappropriate and useless since no living bacteria are involved in this presentation of disease. Use of antitoxins would be the method of choice for intervention. B. anthracis (choice A) causes anthrax by bacterial spores entering small abrasions in oral mucosa and germinating into vegetative bacteria. Antibiotics would be the treatment of choice in a clinical situation, although vaccines are available for domestic animals. The other three choices (C, D, and E) all include clostridial organisms that cause diseases where antibiotic treatment is necessary.

QUESTION 394
A foul-smelling specimen was obtained from a 26-year-old female with a pelvic abscess. Culture grew both aerobic and anaerobic gramnegative bacteria. Which of the following represent the cultured organisms?

A. A. israelii and E. coli
B. B. fragilis and L. monocytogenes
C. B. fragilis and N. gonorrhoeae
D. C. difficile and B. fragilis
E. E. coli and Peptostreptococcus spp.

Correct Answer: C
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
Medically important infections due to anerobic bacteria are common. The infections are often polymicrobic, being mixed with other anerobes, facultative anerobes, and aerobes. Anerobes are found in all parts of the body including skin, intestinal tract, oral cavity, and urogenital mucosa. Infection usually occurs when anerobes contaminate usually sterile body sites or are heavily inoculated with anerobes. Most of the B. fragilis bacteria contain small amounts of catalase and SOD, allowing them to survive oxygen toxicity. Their usual clinical manifestation is an abscess. Anerobes produce an extremely foul odor from abscess pus or growth on media. In this scenario, choice C could be the proper answer. A. israelii (choice A) is anerobic but not usually involved in intra-abdominal/pelvic abscess formations. L.

monocytogenes (choice B) enters the GI tract by ingestion of contaminated food (cheese or vegetables). L. monocytogenes is usually found in intrauterine infections, bacteremias, and CNS infections. C. difficile (choice D) is usually present in small numbers and increases when broad- spectrum antibiotics have been used with the patient. C. difficile produces toxins that act on the intestinal lining, producing severe diarrhea. Peptostreptococci (choice E) are anerobic streptococci, usually found in the intestine. These and E. coli would not likely to be routinely found as etiologic causes of pelvic abscesses.

QUESTION 395
A 33-year-old male who practices veterinary medicine in Fresno (central California) is seen in the emergency room with chills, high fever, persistent unproductive cough, and generalized malaise. Physical examination reveals no evidence of pharyngitis, sinusitis, or otitis media. The patient does not have a rash and vehemently proclaims that he has not been bitten by any vectors. On his 10-acre farm, he raises sheep, chickens, turkeys, ostriches, and emus. Acomplement fixation assay for Coxiella is negative. Given the PE and history, which of the following is the most likely etiologic agent?

A. C. pneumonia
B. C. psittaci
C. C. trachomatis
D. Ehrlichia canis
E. Rickettsia typhi

Correct Answer: B
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
The term "psittacosis" is applied to the human disease acquired from contact with birds. "Ornithosis" is applied to infections associated with all types of domestic and free-living birds. In humans, C. psittaci (choice B) produces a range of clinical manifestations ranging from severe pneumonia and sepsis to mild, inapparent infection. A sudden onset of illness taking the form of influenza or nonbacterial pneumonia in a person exposed to birds is suggestive of psittocosis/ornithosis. Such infections will respond to tetracycline treatment. C. trachomatis (choice C) is transmitted person to person and is associated with ocular, genital, and some respiratory infections. C. pneumonia (choice A) is the newest chlamydia species which usually presents with asymptomatic or mild illnesses. Ehrlichiae (choice D) are small, gram-negative bacilli (similar to rickettsiae) that cause nonspecific disease symptoms, fever, chills, headache, vomiting, weight loss, with few reports of respiratory problems. R. typhi (choice E) causes endemic typhus with symptoms similar to those of choice D. Rickettsiae are usually transmitted by insect vectors.

QUESTION 396
S-pyogenes, Group A, is subdivided into specific antigenic types principally on the immunologic differences in which of the following?

A. hyaluronic acid capsule
B. M protein
C. streptolysin O
D. streptolysin S
E. TSST

Correct Answer: B
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
M protein (choice B) is a major virulence factor of Group AS. pyogenes. M proteins appear as hair-like projections of the cell wall which resist phagocytosis by PMNs. Group A Streptococci are nonvirulent, and antibodies to specific M proteins will protect against reinfection. There are, however, more than 80 types of M protein, with little cross-protection observed. M protein may well have an important role in the pathogenesis of rheumatic fever. Purified streptococcal cell wall membranes induce antibodies that cross-react with human cardiac sarcolemma. Acomponent of the cell wall of selected M types induces antibodies that react with cardiac muscle tissue. The M protein serotypes are used to subdivide Group A streptococci into 80 different serotypes. The other choices (A, C, D, and E) are all virulence factors of Group Astreptococci, but do not form the basis of identifying antigenic different subgroups or serotypes.

QUESTION 397
A 39-year-old man with normal sexual practices saw his doctor, complaining of a mild (38.5℃) but pers istent fever. His physician observed pharyngitis and a bilateral conjunctivitis that the patient claimed was recent and painful. Which of the following microbes most likely caused the infection?

A. adenovirus
B. C. pneumoniae
C. N. gonorrhoeae
D. S. pyogenes
E. Toxoplasma gondii

Correct Answer: A
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
Adenoviruses are a frequent cause of infection characterized by a triad of symptoms, namely, pharyngitis, conjunctivitis, and fever. S. pyogenes (choice D) causes 25% of cases of pharyngitis. However, the disease is often accompanied by tonsillitis. The infection is usually associated with fever which is higher than 39℃. N. gonorrhoeae (choice C) normally causes gonorrhea. C. pneumoniae (choice B) causes generally primary atypical pneumonia which is not usually associated with conjunctivitis. T. gondii (choice E) in AIDS patients, or other immunosuppressed individuals can cause disseminated disease and encephalitis (choice E).

QUESTION 398
An elderly patient was hospitalized with severe flu. An enveloped virus was isolated from this patient. Which of the following pertains to this RNA virus with a segmented, negative-sense genome?

A. can have direct viral genome and host cell ribosome interaction
B. cannot possess a lipid envelope
C. must contain a DNA-dependent RNA polymerase
D. must contain an RNA-dependent DNA polymerase
E. must contain an RNA-dependent RNA polymerase

Correct Answer: E
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
The patient was hospitalized due to severe influenza symptoms, and an influenza virus was isolated from clinical specimen. Isolation of the etiologic virus would not change the way medical care was being given to the individual. Influenza viruses have an RNA genome comprising of eight segments, each coding for one or more viral components. Influenza viral genomes are also negative-sense, meaning that within the virus particle, there must be an RNA-dependent RNA polymerase to allow the virus growth cycle to make viral mRNA and viral genomic RNA (choice E). There would be no use for a DNA-dependent RNA polymerase (choice C) or an RNA-dependent DNA polymerase (choice D). Since the influenza virus uses the host cell as a factory to produce new viral progeny, host cell ribosomes would be utilized for viral protein production (choice A) but by definition, negative-sense RNA cannot act as mRNA. Therefore, RNA from the virion could not directly interact with host cell ribosomes. Influenza viruses possess a well-defined lipid envelope (choice B), where the HA and NAglycoproteins are found.

QUESTION 399
Autoantibody testing of a patient with an autoimmune disorder reveals high titers of antibodies against the core proteins of small nuclear ribonucleoprotein particles (Smith antigen). Based on this finding, detection of which of the following is the most important initial clinical feature of this autoimmune disorder?

A. a lesion known as erythema chronicum migrans
B. a rash in a butterfly distribution on the face
C. antibody to single-stranded RNA
D. carditis
E. pneumonitis

Correct Answer: B
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
The autoimmune disease described here by the presence of anti-Sm antibodies is Systemic lupus erythematosus (SLE). This autoimmune disease is initially recognized clinically by a rash on the face with a "wolf"-like shape and thus the name lupus. Such a butterfly rash (over the malar eminences of the face, hence a malar rash) is considered a distinctive manifestation of SLE. The development of erythema chronicum migrans is a pathognomonic feature of Lyme disease

(choice A). Detection of antibodies to double-stranded DNA are pathognomonic for SLE (choice C). Arthritis, but not carditis (choice D) or pneumonitis (choice E), occurs frequently.

QUESTION 400
A newborn has a temperature of 103℉. Blood culture grows out gram-positive cocci in chains. Which of the following is the causative agent?

A. Group A Strep (S. pyogenes)
B. Group B Strep (S. agalactae)
C. N. meningitides
D. Salmonella species
E. S. pneumoniae

Correct Answer: B
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
The streptococci were divided into multiple groups based upon different soluble carbohydrates isolated from the cell walls. This CHO was antigenic, and R. Lancefield produced antibodies against each of them. She initially identified Groups AG. Almost 95% of streptococcal infections in humans are caused by Group A, S. pyogenes (choice A). S. agalactiae is a representative member of the Group B streptococcous (choice B). They are members of the normal flora of the female genital tract and an important cause of neonatal sepsis and meningitis. They produce beta (clear zone) hemolysis, like the Group A members. They can be identified as Group B on the basis of the CAMP test (positive) and monoclonal antibody screening tests. It is important to identify and treat such neonatal infections properly to avoid mortality of the small patients. While N. meningitidis (choice C) may affect infants, most cases of meningitis caused by the organism would be in 5-yearold to young adult patients. Salmonella species (choice D) is an inappropriate choice for thisage and disease. S. pneumoniae (choice E) can affect all age groups, but the highest incidence for meningitis is in the elderly population.

QUESTION 401
Aspecimen of thick, bloody sputum from a hospitalized 80-year-old patient with chronic obstructive pulmonary disease is sent for laboratory analyses. The tests yield heavy growth of a lactose-positive, nonmotile, gram-negative rod with a large gelatinous capsule. Which of the following is this bacterium most likely to be?

A. E. coli
B. Enterobacter aerogenes
C. K. pneumonia
D. P. aeroginosa
E. Y. pseudotuberoulosis

Correct Answer: C
Section: Microbiology/Immunology

Explanation

Explanation/Reference:
Explanation:
K. pneumoniae (choice C) is present in the respiratory tract and feces of about 5% of normal individuals. It causes a small proportion (about 1%) of bacterial pneumonias. It is a gram-negative rod with a well-defined capsule that helps to resist phagocytosis by PMNs. It can produce extensive hemorrhagic necrotizing consolidation of the lung in debilitated patients and can cause nosocomial (hospital acquired) infections. Elderly patients with COPD are particularly at risk with this organism. Other enteric (choices A and B) may also produce pneumonia but do not have the well-defined capsule that K. pneumoniae possesses. P. aeruginosa (choice D) is a widely distributed gramnegative bacillus that can also be quite opportunistic for individuals with abnormal host defenses. P. aeruginosa produces pigments that produce bluegreen pus and is especially a problem with cystic fibrosis patients where the organism resides in a well-defined biofilm within the patient. Y. pseudotubeculosis (choice E) resides in domestic farm animals and is the source of human infections.

QUESTION 402
A 14-year-old boy presents with acne with inflamed follicles and sebaceous glands. Gram stain of a pustule from his face reveals pleomorphic gram-positive bacilli. Which of the following is the organism implicated in this condition?

A. C. durum
B. Erysipelothrix rhusiopathiae
C. L. monocytogenes
D. S. aureus
E. S. epidermidis

Correct Answer: A
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
The non-spore forming gram-positive bacilli are a diverse group of bacteria. While C. diphtherae is the most important pathogen, many corynebacteria and propionibacteria (anerobes) are members of the normal flora of skin and mucus membranes. These bacteria tend to be clubbed or irregularly shaped. C. durum (choice A) is a diphtheroid, a normal flora species that can be opportunistic in the right location, such as hair follicles and sebaceous glands. It may contribute to lesion development or be part of a mixed culture of skin bacteria present in the pustule. E. rhusiopathial (choice B) causes disease in domestic swine. Erysipelas in humans is caused by Group A streptococci. L. monocytogenes (choice C) enters the body through the GI tract after ingestion of contaminated cheese or vegetables. S. aureus (choice D) and S. epidermidis (choice E) are welldefined gram-positive cocci.

QUESTION 403
A Gram stain smear of spinal fluid from a 2- year-old child reveals short gram-negative rods. Which of the following most likely is the organism?

A. A. israelii
B. B. fragilis

C. E. coli
D. H. influenza
E. L. monocytogenes

Correct Answer: D
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
Haemophilus species are a group of small gram-negative pleomorphic bacteria thatrequire blood agar enriched with X and/or V factors for isolation. H. influenzae (choice D) is an important pathogen found on the mucus membranes of the upper respiratory tract in humans. It is an important cause of meningitis in children, and it would not be unusual to isolate the organism from spinal fluid in such a case. Children aged 6 months5 years are the group most at risk. H. influenzae is also able to cause respiratory tract infections in children and adults. Such infections can be controlled by use of the H. influenzae type b conjugate vaccine as part of the pediatric vaccination series. Actinomyces (choice A) species are gram-positive rods, usually found in the oral cavity. B. fragilis (choice B) is a gram- negative rod usually found in the intestinal tract and may be opportunistic. These are anerobes, and appropriate conditions must be used for isolation. E. coli (choice C) is a larger enteric bacterium, also a very efficient opportunist, which will grow on less complex media. L. monocytogenes (choice E) is a grampositive organism.

QUESTION 404
Which pair of organisms below can be routinely responsible for food poisoning?

A. C. botulinum and B. anthracis
B. C. difficile and C. botulinum
C. C. perfringens and B. cereus
D. C. tetani and B. anthracis
E. C. tetani and B. cereus

Correct Answer: C
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
C. perfringens (choice C) may well cause myonecrosis and gas gangrene in an invasive infection due to the many tissue-destroying toxins the bacteria can make. However, a powerful enterotoxin that induces intense diarrhea in 618 hours can be made by C. perfringens. It is similar to food poisoning caused by B. cereus (a soil organism) and tends to be self-limited. B cereus (choice C) produces an emetic type of food poisoning and a diarrheal form by toxins produced by the bacteria. It has a short incubation (hours) and recovery usually occurs in 24 hours. C. botulinum (choice A) produces a toxin that is ingested and affects the CNS in 24 days. Gastrointestinal anthrax (choice A) is quite rare. C. difficile (choice B) become predominant in the intestinal tract as a result of antibiotic treatment. It produces two toxins that cause pseudomembranous colitis. C. tetani (choice D) causes tetanus, not an enteric disease.

QUESTION 405
A number of children are hospitalized with bloody diarrhea and severe hematological abnormalities. A4-year-old girl dies of kidney failure shortly after admittance. Epidemiological investigation establishes that all of the patients developed symptoms soon after consuming hamburgers from the same fast-food restaurant chain. Which of the following organisms is most likely to be responsible for the outbreak?

A. C. jejuni
B. non-01 serogroup of V. cholera
C. O157:H7 serotype of E. coli
D. S. typhimurium
E. Shigella dysenteriae

Correct Answer: C
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
The enterobacteriaceae are a large, heterogeneous group of gram-negative rods that normally inhabit the intestinal tract of humans and animals. The Escherichia genus (usual flora) can incidentally cause disease while Salmonella and Shigella genera are regularly pathogenic for humans. E. coli is the most common cause of urinary tract infection, but there are also several E. coli-associated diarrheal diseases that occur worldwide. Enterohemorrhagic E. coli (EHEC) produces verotoxin and is associated with hemorrhagic colitis and hemolytic uremic syndrome. E. coli serotype O157:H7 (choice C) is the most common strain for these disease presentations. Many outbreaks could be prevented by thoroughly cooking ground beef. EPEC is a strain that causes diarrhea in infants while ETEC is a common cause of traveler's diarrhea. C. jejuni (choice A) can be responsible for a shigella-like illness that is self- limited. Milk or undercooked fowl are frequent vectors of this organism. Non- 01 serogroup of V. cholerae (choice B) only causes a cholera-like illness occasionally. Salmonella (choice D) enterocolitis can be caused by 1400 serotypes. Nausea, headache, vomiting, and profuse diarrhea with low-grade fever are common and resolve in 23 days. The natural habitat of shigellae (choice E) is limited to the intestinal tract of humans and other primates, where they produce bacillary dysentery.

QUESTION 406
A 14-year-old boy is referred to you for nasal obstruction and frequent nosebleeds. Which of the following is the most likely diagnosis?

A. inverted papilloma
B. juvenile angiofibroma
C. nasal polyps
D. nasopharyngeal carcinoma
E. wegener granulomatosis

Correct Answer: B
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Juvenile angiofibroma is a very vascular tumor originating in the nasopharynx that is typically found in teenage boys and young adult males. It may lead to obstruction and, because of its vascularity, it is a frequent cause of epistaxis. It should be suspected in any teenage boy with frequent epistaxis. Inverted papilloma (choice A) is a benign tumor but is aggressive locally and can erode into surrounding structures. Rather than having an exophytic growth pattern, it grows down (thus inverted) into other structures and may be difficult to excise completely. It can cause unilateral obstruction and occasionally epistaxis but is generally seen in an older age group (50s). Nasal polyps (choice C) are not tumors but edematous growths commonly found in patients with allergic rhinitis. They produce chronic nasal obstruction and a gradual loss of olfaction. Nasopharyngeal carcinoma (choice D) is associated with Epstein-Barr virus and is another potential cause of obstruction and hemorrhage but again is seen in older patients. Wegener granulomatosis (choice E) is a necrotizing granulomatous vasculitis involving the nose sinuses, lungs, and kidneys. It occurs most frequently in the fifth and sixth decades.

QUESTION 407
A 57-year-old woman had her last menstrual period at the age of 46. However, for the past 4 months she has experienced intermittent vaginal hemorrhage. A right ovarian mass is identified. Which of the following is the most likely diagnosis?

A. arrhenoblastoma
B. Brenner tumor
C. dysgerminoma
D. granulosa cell tumor
E. Sertoli-Leydig cell tumor
F. teratoma

Correct Answer: D
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
An ovarian mass raises the possibility of a tumor and vaginal hemorrhage in a postmenopausal woman and suggests an estrogenproducing tumor. One of the first estrogenproducing tumors to consider is granulosa cell tumor. Arrhenoblastoma (Sertoli-Leydig cell tumor) (choice A) secretes androgens, not estrogens. Brenner tumor (choice B) is an uncommon ovarian neoplasm without hormonal activity. Dysgerminoma (choice C) is the female counterpart of the male seminoma and does not produce hormones. Sertoli-Leydig cell tumor (choice E) is a synonym for arrhenoblastoma (choice A).
Teratoma (choice F) is also hormonally inactive.

QUESTION 408
A 28-year-old recently divorced man with no significant past medical history presents to the emergency room with progressive lower abdominal pain and cramping over the past 4 days, both of which are relieved by defecation. He has suffered from substantial bloody and mucoid diarrhea during this time. His temperature is 102.8℉. Laboratory studies reveal an elevated whit e blood cell (WBC) count and a high erythrocyte sedimentation rate. Sigmoidoscopy reveals extensive rectal and sigmoid hyperemia and edema, numerous superficial ulcerations, and small focal mucosal hemorrhages, many of which have suppurative centers. Significant

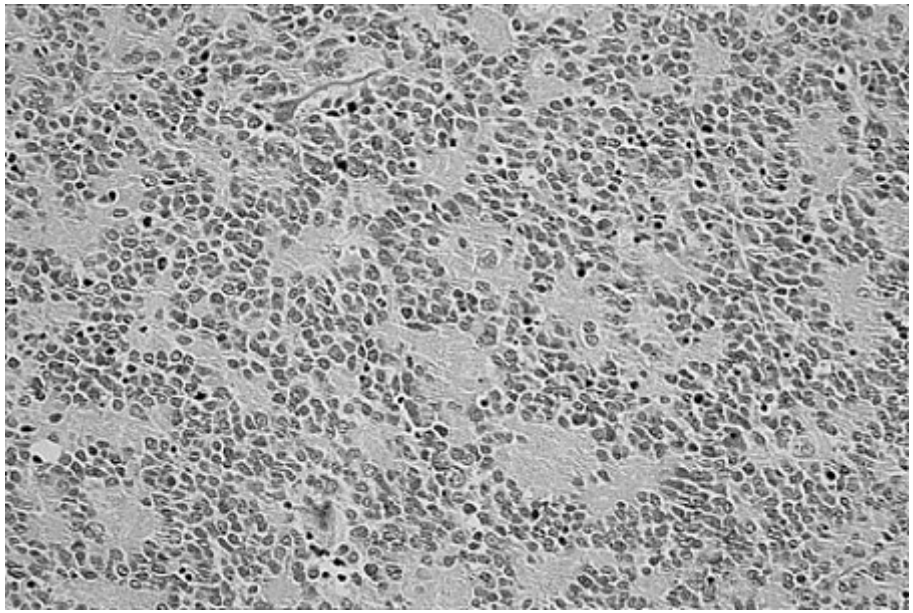
intestinal narrowing is seen in the distal transverse colon. These findings most likely suggest a diagnosis of which of the following?

A. amebic colitis
B. collagenous colitis
C. cytomegalovirus enterocolitis
D. pseudomembranous colitis
E. ulcerative colitis

Correct Answer: E
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Clinical history and sigmoidoscopy findings are consistent with a diagnosis of ulcerative colitis, an idiopathic inflammatory bowel disease that involves the rectum in virtually all cases and extends proximally in a continuous manner without skip lesions to include variable lengths of the colon. Psychological stress (recent divorce) may serve to precipitate acute attacks of the disease. The significant narrowing seen in the transverse colon in this patient suggests the possible progression to toxic megacolon, a rare complication in severe acute disease that carries a high mortality rate and requires emergency colectomy. Amebic colitis (choice A) is characterized by acute inflammation with multiple areas of enzymatic tissue necrosis leading to submucosal, flask-shaped abscesses throughout the colon. Clinical features include bloody and mucoid diarrhea with low-grade fever. Collagenous colitis (choice B) is a more recently recognized form of colitis characterized clinically by episodic or chronic watery diarrhea that is not severe enough to cause dehydration, and pathologically by the presence of a distinct collagenous band beneath the colonic surface epithelium. Patients very often have a variety of autoimmune and other diseases. Cytomegalovirus enterocolitis (choice C) is a common GI infection in acquired immunodeficiency syndrome (AIDS) patients that infects the entire GI tract and produces severe, chronic diarrhea. Both mucosal epithelial and vascular endothelial cells are infected. Vasculitis may result in focal ischemic necrosis of the intestinal wall. Pseudomembranous colitis (choice D) is caused by a necrolytic enzyme produced by Clostridium difficile bacteria that most often proliferate secondary to a variety of antibiotic therapies; clindamycin is a frequent culprit. Diarrhea is most often watery and profuse. Gross findings include patchy areas of mucosal inflammation with multiple, discrete yellowish plaques constituting the pseudomembrane, which is composed of fibrin, mucin, and necrotic debris.

QUESTION 409
A 15-month-old girl presents with a large abdominal mass, weight loss, and fever. At surgery, a large infiltrative tumor with areas of hemorrhage and necrosis is removed. A photomicrograph of a section from this tumor is shown in below figure. Which of the following is the most likely diagnosis?



A. embryonal rhabdomyosarcoma
B. malignant lymphoma
C. neuroblastoma
D. teratoma
E. Wilms' tumor

Correct Answer: C
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
This is a neuroblastoma and is one of a group of childhood tumors described as "small, round, blue-cell tumors," consisting as they do of monotonous small cells with dense, blue nuclei. The characteristic microscopic feature of a neuroblastoma is the pseudorosette, a ring of primitive neuroblasts surrounding a central space filled with fibrillar extensions from the cells. Many of these can be seen in figure. These are called pseudorosettes because they do not have a central lumen as is found, for example, in the rosettes in retinoblastoma. Embryonal rhabdomyosarcoma (choice A) is a type of rhabdomyosarcoma typically found in children under the age of 10. It can arise in a number of locations and sarcoma botryoides is one form. It does not form rosettes. Malignant lymphomas (choice B) and leukemias are together the most common malignancies of childhood in the United States, but rosette formation is not a distinctive microscopic feature. Teratomas (choice D) in infants and young children are usually benign tumors found in the midline (e.g., sacrococcygeal, mediastinal). They are composed of tissues with a normal

histologic appearance derived from all three germ layers. Wilms' tumor (choice E) or nephroblastoma is derived from primitive blastema cells and sometimes displays aborted attempts to form glomeruli or renal tubules, but not rosettes.

QUESTION 410
A 52-year-old woman presents to her primary care physician complaining of increasing fatigue and mild shortness of breath. Blood work reveals a hypochromic anemia with a hemoglobin concentration of 10.4 g/dL, MCV of 76 / , MCHC of 29 g/dL, and a decrease in the absolute reticulocyte count.

m^3

WBC and platelet counts are within normal limits. Serum iron and ferritin levels are low and total iron- binding capacity is elevated. Which of the following conditions best accounts for these findings?

A. anemia of chronic disease
B. aplastic anemia
C. hypothyroidism
D. iron deficiency
E. pernicious anemia

Correct Answer: D
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Laboratory findings of a hypochromic anemia with a decrease in MCV and MCHC indices and a decreased reticulocyte count suggest a hypoproliferative anemia. The various microcytic, hypochromic anemias belong to this category and a partial differential diagnosis for these includes iron-deficiency anemia, anemia of chronic disease (ACD) (choice A), thalassemias, and sideroblastic anemias. ACD (choice A) may be distinguished from irondeficiency anemia by additional iron studies, as were performed in this case. While serum iron and ferritin levels are low and total ironbinding capacity (TIBC) is elevated in irondeficiency anemia, in ACD ferritin is typically normal or elevated, iron is low, and TIBC is low. ACD is associated with a functional, not an absolute, deficiency in iron as a result of sequestration by reticuloendothelial cells. Aplastic anemia (choice B) causes a pancytopenia, which was not the case in this patient as WBC and platelet levels were normal. Hypothyroidism (choice C) and pernicious anemia (choice E) are megaloblastic anemias, which demonstrate increased, not decreased, MCV values (~ >110 fL).

QUESTION 411
A 52-year- oldwoman has had rheumatoid arthritis for many years. She now comes to you complaining of the development in the past few months of redness, burning, and itching of her eyes and a dry mouth, making swallowing difficult. This newly developing condition gives the patient a greatly increased risk for which of the following?

A. esophageal carcinoma
B. leukemia

C. lymphoma
D. melanoma
E. pleomorphic adenoma

Correct Answer: C
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Sjögren syndrome is an autoimmune disease in which there is immune-mediated destruction of lacrimal and salivary gland epithelium leading to diminished secretion by these organs. This disease may occur as a primary disorder or more commonly secondary to another autoimmune disorder, such as rheumatoid arthritis, as seen in this patient. One of the long-term risks for Sjögren syndrome is a 40- fold increase in malignant lymphoma. The development of esophageal carcinoma (choice A) is associated with alcohol use, smoking, Barrett metaplasia, and Epstein-Barr virus infections. Chronic Sjögren syndrome is not known to cause an increased incidence of leukemia (choice B). Melanoma (choice D) is a malignancy of melanocytes unrelated to Sjögren syndrome. Pleomorphic adenoma (choice E) is a benign salivary gland tumor composed of both neoplastic epithelium and stroma. Its occurrence is not associated with Sjögren syndrome.

QUESTION 412
A 3-year-old girl develops gastroenteritis and a number of other children at the day care nursery that she attends are also affected. This was most likely caused by which of the following agents?

A. Balantidium coli
B. Cryptosporidium parvum
C. Entamoeba histolytica
D. Giardia lamblia
E. rotavirus

Correct Answer: E
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Rotavirus is the most common cause of severe diarrhea worldwide and is most widespread in very young children. It is passed readily to others and can result in outbreaks such as described here. B. coli (choice A) is a ciliated intestinal protozoal parasite that is found mostly in the tropics. It is a rare cause of diarrhea in the United States. C. parvum (choice B) is a spore-forming protozoan that can cause severe diarrhea in immunocompromised individuals. E. histolytica (choice C) is another protozoan parasite. It infests the colon forming flask-shaped ulcers (i.e., having narrow neck and a wide base that undermines the adjacent mucosa). These organisms can also be carried in the portal circulation to the liver where they form characteristic "anchovy paste" abscesses. G. lamblia (choice D) is an intestinal flagellate that infests the upper small intestine. It is very common worldwide and is the most common intestinal protozoan parasite in the Western world. The majority of infected individuals remain asymptomatic but it can cause diarrhea that is usually mild but can be severe.

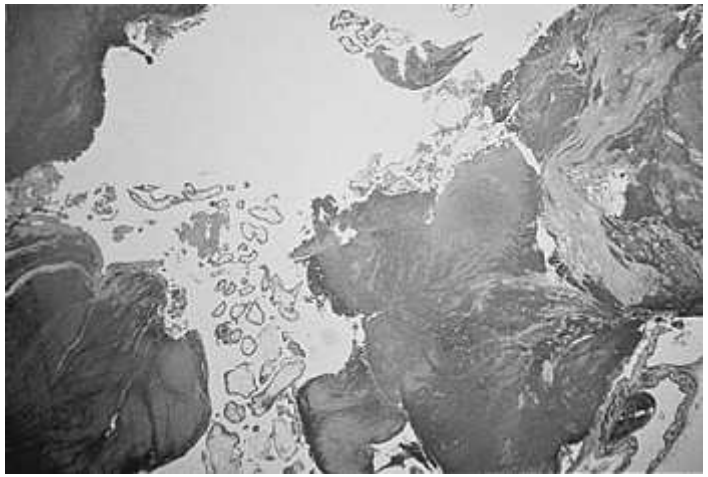
QUESTION 413
A 9-year-old boy is stung on the arm by a wasp and very rapidly develops redness and swelling at the site of the sting. Which of the following substances is most responsible for these early changes?

A. bradykinin
B. complement 3a
C. histamine
D. leukotriene
E. thromboxane

Correct Answer: C
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Histamine is a preformed inflammatory mediator found principally in mast cells and basophils that has a major role in the early vascular changes of inflammation; that is, dilation of precapillary arterioles which produces the local redness (rubor) and warmth (calor), and the increased permeability of postcapillary venules which produces the swelling (tumor). Bradykinin (choice A) has similar effects to histamine, but it is produced by the activation of the kinin system so it is not immediately available as is histamine. Complement 3a (choice B) and complement 5a are called anaphylatoxins because they can stimulate the release of histamine from mast cells. Leukotriene B4 (choice D) is a major activator and chemotactic agent for leukocytes and potentiates their adhesion to vessel walls. Thromboxane A2 (choice E) promotes platelet aggregation and vasoconstriction; it functions in opposition to prostaglandin, which inhibits platelet aggregation and causes vasodilation.

QUESTION 414
A 21-year-old woman presents with a 6-hour history of left-sided lower abdominal pain and is found to be hypotensive. A hemorrhagicmass is discovered in her left fallopian tube during laparoscopy. The tube is surgically excised. A photomicrograph of the tubal contents is displayed in below figure. Which of the following is the most likely diagnosis?



A. chorioadenoma destruens
B. choriocarcinoma
C. ectopic tubal pregnancy
D. granular cell tumor
E. leiomyoma

Correct Answer: C
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
figure displays viable benign chorionic villi that are diagnostic of an ectopic tubal pregnancy. The clinical history of acute lower abdominal pain and hypotension are expected findings with an ectopic pregnancy. Chorioadenoma destruens (choice A) is also referred to as invasive mole, and would display invasion of chorionic elements into the uterine, not tubal, muscular layers. Choriocarcinoma (choice B) is a malignant neoplasm composed of gestational trophoblastic tissue. Figure displays benign chorionic elements. Granular cell tumor (choice D) is a neoplasm of neuraltype tissue. The photomicrograph is incompatible with this diagnostic consideration. Leiomyomas (choice E) rarely occur in the fallopian tube. They are most commonly seen in the wall of the uterus. Bundles of benign smooth muscle cells are seen microscopically.

QUESTION 415
A 45-year-oldman is admitted to the hospital for elective gastrointestinal surgery. On the third post- operative day, the patient experiences a fever of 101.5℉, and reports having a slight cough, but is otherwise asymptomatic. Chest x-ray demonstrates a small, interstitial infiltrate in the left lower lobe. Three sets of blood cultures (two bottles each) are drawn and sent to the laboratory. Culture results report positive Staphylococcus epidermidis growth from one bottle of the first culture set, and negative growth from the second and third culture sets. Based on this information, which of the following is the best interpretation of these blood

culture results?

A. intermittent bacteremia associated with postsurgical abscess formation
B. postoperative septicemia secondary to infective endocarditis
C. postoperative septicemia secondary to pneumonia
D. postoperative septicemia secondary to surgical manipulation of the gastrointestinal tract
E. skin flora contamination and not septicemia

Correct Answer: E
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
True positive blood cultures are defined by positivity in multiple cultures in a series, whereas contaminates generally are not found in repeat cultures. For example, finding S. epidermidis (found in normal skin flora) in only one bottle of six in three blood culture sets (as in this patient) most probably represents skin contamination. If, however, S. epidermidis were isolated from all six bottles drawn from a patient suspected of having infectious endocarditis, this would be interpreted as a true positive. Thus, the results do not support a diagnosis of either bacteremia or septicemia (choices A through D).

QUESTION 416
A 32-year-old man is admitted for neuropsychiatric evaluation after exhibiting bizarre behavior. During his medical workup, he is found to have cirrhosis and a mild parkinsonian tremor. Which of the following diagnoses provides the best explanation for these findings?

A. congenial hepatic fibrosis
B. peliosis hepatis
C. primary sclerosing cholangitis
D. Reye syndrome
E. Wilson disease

Correct Answer: E
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Wilson disease is an autosomal recessive disorder of copper metabolism due to defective biliary excretion of the copper-protein complex ceruloplasmin. Cells of the liver and brain, notably the basal ganglia, are particularly vulnerable to the toxic effects of excessive copper accumulation. Treatment with copper chelating agents, such as penicillamine or triethylene tetramine, has a dramatically beneficial effect. Congenital hepatic fibrosis (choice A) is a rare disorder of unknown etiology. It is most prevalent in India. Peliosis hepatis (choice B) is a rare hepatic circulatory disorder caused by dilation of sinusoids, resulting in small, blood-filled

spaces within the liver; the condition is typically asymptomatic. Steroid hormone usage is associated with its development in some instances. Primary sclerosing cholangitis (choice C) is due to chronic inflammation and fibrosis of intra- and extrahepatic bile ductules. The etiology is obscure. Most of those affected also have ulcerative colitis. Reye syndrome (choice D) refers to acute hepatic failure in children following ingestion of aspirin for certain upper respiratory illnesses, particular influenza, or chickenpox.

QUESTION 417
A 26-year-old man presents with a 3-week history of increasing pain just below his right knee. He does not recall sustaining any trauma to his leg and is not experiencing pain elsewhere; he states that he is otherwise healthy. Examination reveals only tenderness to palpation in the area. An x-ray of his right knee demonstrates a small lytic lesion in the tibial medial condyle surrounded by a focus of sclerosis. Based on this information, what is the most likely diagnosis?

A. gout
B. osteochondroma
C. osteomyelitis
D. osteosarcoma
E. rheumatoid arthritis

Correct Answer: C
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Bacteria are the principle cause of osteomyelitis, infecting bone either by direct penetration (e.g., puncture), extension from a surrounding area (e.g., cellulitis), or via hematogenous spread of an overt infection (e.g., sinusitis, pneumonia) or an occult bacteremia (e.g., mouth, intestinal flora); the leading causative pathogen is S. aureus. Long bone metaphyses are commonly infected in children, whereas long bone epiphyses and vertebrae are more typically affected in adults. Presentation may be limited to pain, with or without fever. The classic x-ray findings include lytic changes caused by necrotic bone (sequestrum) and sclerosis due to the ingrowth of fibrous tissue as new bone growth (involucrum) forms around the devitalized bone. Gout (choice A) is associated with hyperuricemia, leading to acute synovial inflammation and deposition of urate crystals in joint spaces; similarly, rheumatoid arthritis (choice E) is an autoimmune disorder affecting the synovial lining of various joints (chronic synovitis). Osteosarcomas (choice D) are typically large, bulky malignancies most commonly originating in long bone metaphyses, often with secondary spread into epiphyseal regions. Osteochondromas (choice B) are benign tumors arising near the growth plate in endochrondrally derived long bones which form bony, pedunculated, cartilage-capped lesions.

QUESTION 418
A 63-year-old woman has a routine chest x-ray that reveals a suspicious subpleural lesion. The lesion is resected and sectioned, and reveals all (choices A through F) of the following microscopic findings. Which of these findings would most strongly indicate that the lesion is a malignant neoplasm?

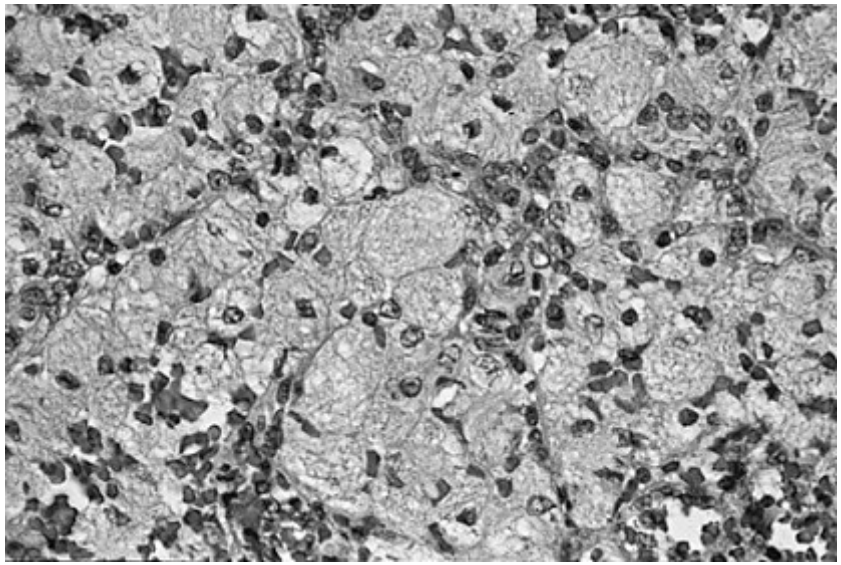
A. hyperchromatism
B. increased nuclear/cytoplasmic ratio
C. invasion
D. mitoses

E. necrosis
F. pleomorphism

Correct Answer: C
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
One might see all of these microscopic findings in a malignant neoplasm, but invasion is the strongest indicator. Hyperchromatism (choice A) is a typical finding in malignant cells indicating their increased DNA content. However, it is not a reliable marker for malignancy. Increased nuclear/cytoplasmic ratio (choice B) can also be seen as part of the normal proliferative response. Mitoses (choice D) indicate an increased proliferative rate, but again the proliferation is not necessarily neoplastic. Necrosis (choice E) is often a feature of rapidly dividing tumors but is also found with infarction, infection, and other conditions. Pleomorphism (choice F) is another feature that is common in malignant tumors, but it can be seen in nonneoplastic conditions and there are some malignancies that are fairly monomorphic.

QUESTION 419
The bone marrow biopsy depicted in below figure was obtained from an infant with hepatosplenomegaly and mental retardation. The pathologic basis of this disorder is best explained by which of the following?



A. deficient cellular immunity that permits continued intracellular bacterial proliferation

B. exposure to excessive radiation during embryogenesis
C. hereditary defect of a catabolic enzyme leading to abnormal intracellular accumulation of lipids
D. oncogenic viral integration into host's DNA that initiates unregulated cellular proliferation
E. traumatic injury during delivery

Correct Answer: C
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
figure depicts macrophages filled with lipids from an infant with Gaucher disease. The disease is due to a genetic lack of the catabolic enzyme glucocerebrosidase, which fosters the abnormal accumulation of glucocerebroside within the reticuloendothelial cells and neurons. Gaucher disease is not caused by deficient cellular immunity (choice A), radiation (choice B), viral infection (choice D), or trauma (choice E).

QUESTION 420
A 72-year-oldman with a known history of chronic essential hypertension dies unattended at home. The medical examiner determines the cause of death to be hypertensive intracerebral hemorrhage. The most likely site of the hemorrhage is which of the following?

A. basal ganglia or thalamus
B. cerebellum
C. frontal lobe
D. occipital lobe
E. pons

Correct Answer: A
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
About 65% of hypertensive intracerebral hemorrhages occur within the basal ganglia or thalamus. Chronic hypertension predisposes to weakening of arteriole walls with subsequent production of CharcotBouchard aneurysms. A rupture of these aneurysms frequently results in fatal intracerebral hemorrhage. The cerebellum (choice B) is the site of hypertensive hemorrhage about 8% of the time. Hypertensive hemorrhages are very rare in the frontal lobe (choice C) and in the occipital lobe (choice D). The pons (choice E) is the site of hypertensive hemorrhage about 15% of the time.

QUESTION 421
Exhibit:

A. A
B. B_1(thiamine)
C. B_{12}(cyanocobalamin)
D. C (ascorbate)
E. D (calciferol)
F. K

Please refer to the exhibit.
A 14-month-old baby boy is brought to your office by his mother because he seems to be in pain whenever he tries to move. During your physical examination you note bowing of his legs, depression of the sternum with outward projection of the ends of the ribs, reluctance to move his limbs, and numerous bruises on his legs as well as gingival hemorrhages. These findings lead you to suspect that this child suffers from a dietary deficiency of which of the following vitamins?

A. A
B. B
C. C
D. D
E. E
F. F

Correct Answer: D
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Deficiencies of vitamin C and vitamin D can produce similar skeletal abnormalities in young children such as those listed. However, a major difference is that vitamin C deficiency is accompanied by hemorrhages, as seen in this child. This also leads to hemarthrosis (bleeding into joints) that makes movement very painful. Vitamin A deficiency (choice A) is associated with night blindness, with or without keratomalacia and papular dermatitis. Vitamin B1 deficiency (choice B) produces beriberi marked by polyneuropathy, heart failure, and edema (or Wernicke syndrome in chronic alcoholics). Vitamin B12 deficiency (choice C) produces megaloblastic anemia and subacute combined degeneration of the spinal cord. Vitamin D deficiency (choice E) produces osteomalacia in adults and rickets in children due to defective mineralization of bone. Vitamin K deficiency (choice F) can result in a bleeding diathesis because it is required for the activity of clotting factors II, VII, IX, and X.

QUESTION 422
A 10-year-old boy is brought to a pediatric clinic by his mother, who states that he has been voiding brown-colored urine for the past 2 days. The child's history is negative except for a sore throat about 2 weeks ago. Physical examination reveals moderate periorbital edema and mild hypertension. Urinalysis demonstrates red

cells, both red and white cell casts, and 2+ protein. If a renal biopsy were obtained, what would be the characteristic light and/or electron microscopic finding in the glomeruli?

A. hypercellularity with duplication of the basement membrane
B. hypercellularity with subepithelial "humps"
C. hypercellularity with "wire loop"lesions
D. normocellularity with effacement of epithelial cell foot processes
E. normocellularity with segmental sclerosis
F. normocellularity with thickened basement membranes

Correct Answer: B
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Acute postinfectious (poststreptococcal) glomerulonephritis occurs more commonly in young children following a sore throat or, less frequently, a skin infection. They usually present with mild periorbital edema, mild to moderate hypertension, and urinary changes. Urinalysis will show hematuria, mild proteinuria, and red and white cells casts. Light microscopy of a renal biopsy will reveal hypercellularity due to proliferation of endothelial and mesangial cells and the infiltration of neutrophils and monocytes. Immune complexes are deposited in the subepithelium of the glomerular basement membrane and may be seen as subepithelial "humps" by electron microscopy. Choices A, C, D, E, and F refer to the microscopic findings in membranoproliferative glomerulonephritis type 1, lupus nephritis, nil disease, focal segmental glomerulosclerosis, and membranous glomerulopathy, respectively.

QUESTION 423
A 56-year-old man complains of increasing dyspnea on exertion over the past few days. He is noted to be overweight and cyanotic. He has smoked cigarettes for at least 35 years and has a long-standing history of persistent cough, producing a large amount of thick mucopurulent sputum. Auscultation reveals scattered rhonchi and wheezes. Histological examination of his lung tissue would most likely how which of the following?

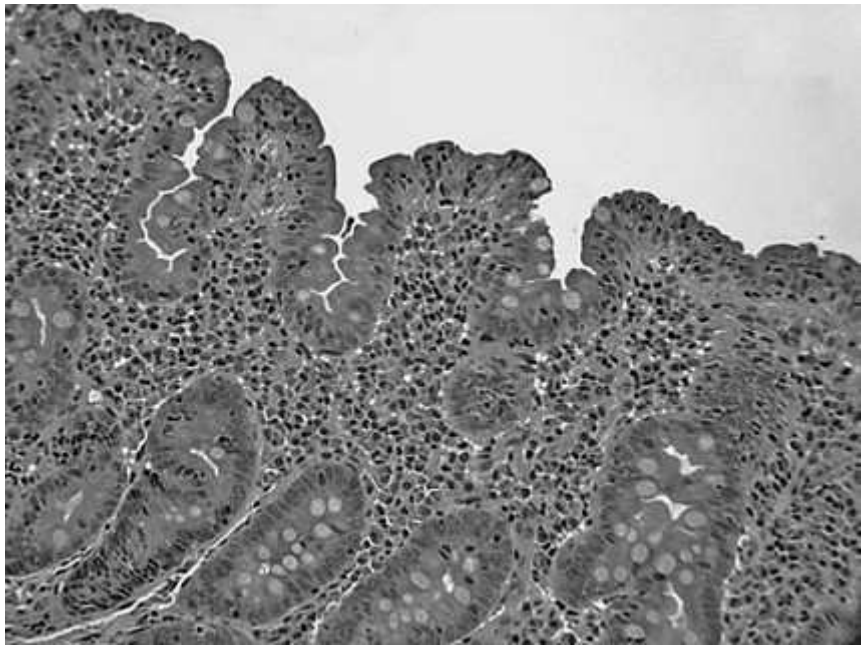
A. expanded alveolar septae infiltrated by mononuclear cells
B. mucous gland hypertrophy and fibrosis of bronchiolar walls
C. neutrophilic exudate occupying the alveoli of an entire lobe
D. pink, proteinaceous layer lining the alveolar spaces
E. thickened basement membranes and many eosinophils

Correct Answer: B
Section: Pathology and Path physiology
Explanation

Explanation/Reference:

Explanation:
This presentation is fairly typical for a patient with chronic bronchitis. Microscopically one would expect to see hypertrophy of bronchial mucous glands accompanied by chronic inflammation and fibrosis of bronchiolar walls. Expanded or thickened alveolar septae infiltrated by mononuclear cells (choice A) would be seen when there is an interstitial response in the lung as, for example, in viral or mycoplasmal pneumonia. Neutrophilic exudate occupying the alveoli of an entire lobe (choice C) is a description of a classic lobar pneumonia. Pink, proteinaceous layer lining the alveolar spaces (choice D) is a hyaline membrane that one might see in shock lung or respiratory distress syndrome. Thickened basement membranes and many eosinophils (choice E) would be seen in asthma.

QUESTION 424
A 6-year-old child presents with diarrhea, malabsorption, and steatorrhea. A photomicrograph from a small intestinal mucosal biopsy is displayed in below figure. An appropriate treatment would be which of the following?



A. alpha-interferon therapy
B. antineoplastic drugs
C. initiation of a gluten-free diet
D. referral to hospice for supportive care
E. surgical resection of a segment of small Bowel

Correct Answer: C

Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
The child has celiac disease, a disorder resulting from a hypersensitivity reaction to gluten in the diet. Withdrawal of gluten from the diet is usually curative. Clinically, there is diarrhea, malabsorption, and steatorrhea. Histologically, there is villous atrophy of the small intestinal mucosa. A referral to hospice for supportive care (choice D) is unlikely to be necessary; more than 95% of patients respond to the removal of gluten from their diet. Recalcitrant cases are rarely life threatening and may be successfully treated with various forms of hyperalimentation that bypass the small intestine. Because the disease is usually cured by dietary measures, the use of alphainterferon therapy (choice A), antineoplastic drugs (choice B), and surgical resection of the small intestine (choice E) are not appropriate treatment options.

QUESTION 425
A 57-year-old man seeks medical attention for the recent appearance of numerous, large, fluid-filled, cutaneous blisters. These involve the face, scalp, neck, and axillae. Manual pressure to the skin results in epidermal separation. These changes are most likely the result of which of the following?

A. autoimmune disorder
B. bacterial infection
C. dietary deficiency
D. exposure to a chemical toxin
E. local ischemia

Correct Answer: A
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Pemphigus vulgaris is an autoimmune disorder. The autoantibodies are directed against keratinocyte antigens with subsequent dyshesion and fluid-filled blister formation. Bacterial infections (choice B), dietary deficiencies (choice C), chemical toxins (choice D), and local ischemia (choice E) are not thought to be the causative agent of pemphigus vulgaris.

QUESTION 426
A 32-year-old male cyclist is struck at night by a hit-and-run motorist. He is unconscious and severely injured and is not discovered until a pedestrian walks by 2 or 3 hours later. When he arrives at the emergency room, he is in shock and his BP is 80/30 mm Hg. He is transfused and a large wound on his right leg is cleaned and sutured. However, by the next day his urine output has decreased to less than 20 mL/h. Which of the following microscopic descriptions best describes his kidneys at this time?

A. acute PMN infiltration of tubules and interstitium
B. fibrinoid necrosis of arterioles

C. focal tubular necrosis with pigmented cellular casts
D. interstitial mononuclear infiltrate with "thyroidization"
E. wedge-shaped areas of coagulative necrosis

Correct Answer: C
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
One of the consequences of shock is hypoperfusion of the kidneys producing ischemia and acute tubular necrosis, which in turn produces acute renal failure. In this patient this was expressed in the greatly reduced urine production. The pigmented casts are formed from Tamm-Horsfall protein and the sloughed tubule cells. Acute PMN infiltration of tubules and interstitium (choice A) may be observed in acute pyelonephritis. Fibrinoid necrosis of arterioles (choice B) is seen in both malignant hypertension and in some vasculitides such as polyarteritis nodosa. Interstitial mononuclear infiltrate with "thyroidization" (choice D) would be an expected finding for chronic pyelonephritis. Wedge- shaped areas of coagulative necrosis (choice E) describe typical renal infarcts.

QUESTION 427
A 76-year-old woman suffers a massive myocardial infarct and dies in cardiogenic shock 20 hours after its onset. Microscopic examination of her infarcted myocardium would be expected to demonstrate which of the following?

A. abundant neutrophils and monocytes
B. coagulative necrosis with few neutrophils
C. fibrosis and collagen deposition
D. monocytes and neovascularization
E. plasma cells and caseous necrosis

Correct Answer: B
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
A 20-hour-old ischemic infarct of the myocardium should demonstrate coagulative necrosis without much of an inflammatory response. Abundant neutrophils and monocytes (choice A) typically are seen about 24 days after an infarction. Fibrosis and collagen deposition (choice C) are late healing phenomena that do not begin until at least 1 week after the infarct has occurred. Monocytic infiltration and neovascularization (choice D) usually occur about 36 days after an infarction. Plasma cells and caseous necrosis (choice E) are not seen with ischemic myocardial damage. Plasma cells are typically seen in areas of chronic inflammation and caseous necrosis is found in granulomas produced in response to tuberculosis and certain fungal infections.

QUESTION 428
A 32-year-old man presents with diarrhea and symptoms of peptic ulcer disease. Endoscopy reveals two ulcers, one in the first portion of the duodenum and one in

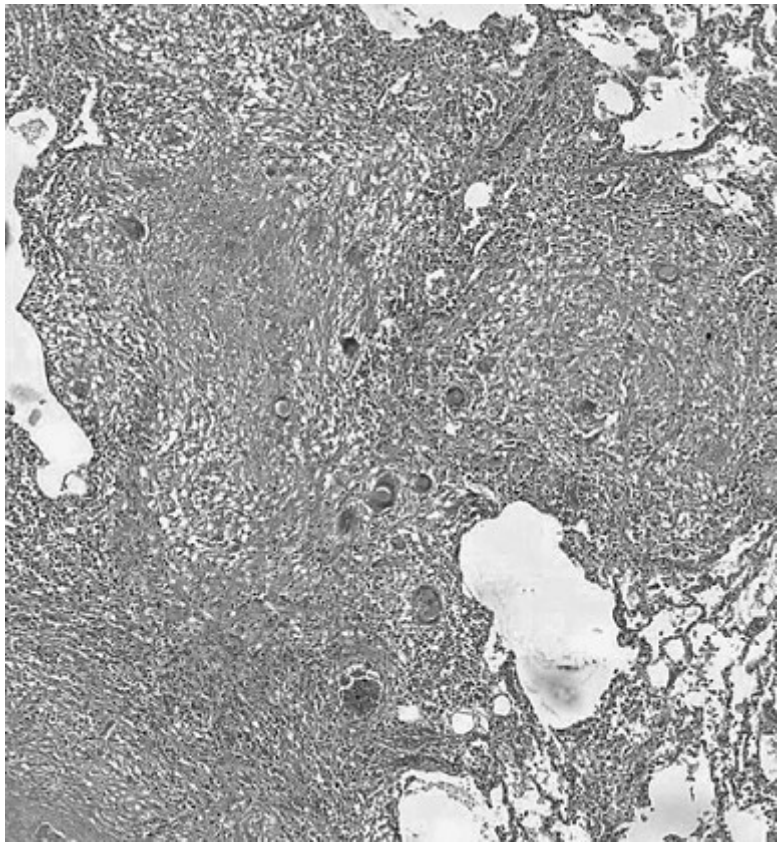
the midduodenum. However, they do not respond to the usual peptic ulcer treatment programs. The most likely explanation for the findings in this patient is which of the following?

A. antibodies to intrinsic factor
B. ectopic hypersecretion of gastrin
C. gastric mucosal atrophy
D. pressure ulceration from bezoars
E. vascular abnormality

Correct Answer: B
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Peptic ulcerations seen in ZollingerEllison syndrome are due to ectopic hypersecretion of gastrin. An islet cell tumor of the pancreas is the most frequent ectopic site. Antibodies to intrinsic factor (choice A) are seen with pernicious anemia and usually cause gastric mucosal atrophy and metaplasia. Gastric mucosal hypertrophy, not atrophy (choice C), is the expected result with an increased secretion of gastrin as is seen with ZollingerEllison syndrome. Pressure ulceration from bezoars (choice D) and vascular abnormalities (choice E) are not the etiology of the peptic ulcerations seen with Zollinger Ellison syndrome.

QUESTION 429
A 47-year-old man has been chronically ill for the past 18 months. He undergoes a lung biopsy and a ection is shown in below figure. Which of the following is the most likely diagnosis?



A. aspergillosis
B. leprosy
C. pneumocystosis
D. sarcoidosis
E. tuberculosis

Correct Answer: E
Section: Pathology and Path physiology
Explanation

Explanation/Reference:

Explanation:
Figure shows a microscopic section of lung in which there are a number of necrotizing granulomas- containing giant cells. Aspergillosis (choice A) and pneumocystosis (choice C) are not associated with granuloma formation. Leprosy (choice B) does (in tuberculoid leprosy) form granulomas and may be found in the upper airways, but does not involve viscera such as the lung. Sarcoidosis (choice D) is a granulomatous disease of unknown etiology that can involve the lung and many other organs but the granulomas are non-necrotizing.

QUESTION 430
A 5-week-old girl, who appeared to be healthy at birth, develops diarrhea and vomiting a few days after birth. Your current examination reveals that she has hepatomegaly, jaundice, and early cataract formation and is not meeting developmental milestones. You suspect that she has which of the following conditions?

A. galactosemia
B. Hurler syndrome
C. pyloric stenosis
D. Tay-Sachs disease
E. type I glycogenosis

Correct Answer: A
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Galactosemia is an autosomal recessive disorder due (in this more common and more severe form of the disease) to a lack of galactose- 1-phosphate uridyl transferase. This results in the formation and accumulation of galactose metabolites. If the infant's diet is not modified to exclude milk products, this will result in damage to the liver (fatty change, cholestasis, cirrhosis, liver failure), eyes (cataract formation), and brain (mental retardation). Hurler syndrome (choice B) is a severe form of mucopolysaccharidosis that typically becomes apparent between 6 months and 2 years of age. Prominent features include coarse facies, dwarfism, organomegaly, cataracts, and mental retardation, not diarrhea, vomiting, and jaundice. Pyloric stenosis (choice C) can occur as a congenital condition, more frequently in baby boys (M:F = 4:1). It is marked by projectile vomiting in the first month of life, but not the other findings in this case. Tay-Sachs disease (choice D) is a lipid storage disease due to a deficiency of hexosaminidase A. There is an inexorable deterioration of mental and motor functions within a few months of birth culminating in a vegetative state and death within 3 or 4 years. Type I glycogen storage disease or von Gierke disease (choice E) is due to a deficiency of glucose-6- phosphatase and usually becomes apparent in the first year of life as hypoglycemia and/or hepatomegaly.

QUESTION 431
A 39-year-old woman reports headaches, weakness and fatigue, and frequent urination over the past several weeks. Physical examination reveals diastolic hypertension. Laboratory findings include hypokalemia and reduced rennin levels. Which of the following is the most likely cause of these various findings?

A. Conn syndrome
B. diabetes insipidus
C. diabetes mellitus
D. pheochromocytoma

E. polycystic renal disease

Correct Answer: A
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Primary aldosteronism caused by an aldosterone-secreting adrenal neoplasm is known as Conn syndrome. Excess aldosterone production leads to increased sodium retention and reciprocal potassium depletion in the renal distal tubule; polyuria results from impairment in urinary concentrating ability. Increased sodium reabsorption and associated extracellular fluid expansion lead to diastolic hypertension and suppression of the reninangiotensin pathway. Muscle weakness and fatigue are a consequence of hypokalemia, which may be severe in some cases. Diabetes insipidus (choice B) is marked by the fairly sudden onset of extreme polyuria and (for the central type) is due to decreased activity of antidiuretic hormone typically associated with an intracranial lesion or trauma. In diabetes mellitus (choice C), glucose levels exceed renal reabsorption capacity, leading to glycosuria and a consequent osmotic diuresis, hypovolemia, and pseudohyponatremia. Pheochromocytomas (choice D) are unilateral, solitary neoplasms most commonly arising from chromaffin cells in the adrenal medulla. Although biologically benign, excessive secretion of catecholamines causes paroxysmal systolic and diastolic hypertension that may reach life-threatening pressures. The adult form of polycystic renal disease (choice E) is an autosomal-dominant condition characterized by grossly enlarged bilateral kidneys containing numerous, and variably-sized expansile cysts. Hematuria, pyelonephritis, hypertension, and polyuria are common symptoms.

QUESTION 432
A 43-year-old woman with a long history of chronic allergies visits her primary care physician with a 2-week history of progressive left perinasal pain and nasal pressure, increasing episodes of yellowish- green nasal discharge, and a fever 1 day prior of 100.8℉. Significant findings on physical examination include a temperature of 101.0℉, tenderness to palpation ove r the left maxillary sinus, and nasal speculum observation of obstruction of the left middle meatus by a large, pale, polypoid mass with a small focus of ulceration and a similar but smaller mass seen in the right middle meatus. A clinical diagnosis of left maxillary sinusitis is made and the patient is started on antibiotics. She is subsequently referred to an otolaryngologist who excises the bilateral masses to relieve the sinus obstruction. Which of the following findings would you expect the pathologist to see on microscopic examination of these masses?

A. hyperkeratotic squamous epithelium with a submucosal core of myxoid connective tissue, frequent blood vessels, mild fibrosis, and a mononuclear infiltrate
B. myofibroblastic proliferation in a dense fibrovascular stroma with numerous endothelial-lined channels
C. papillomatous proliferation of squamous epithelium extending downward through the submucosal connective tissue
D. respiratory epithelium containing an edematous, loose stroma and a mixed inflammatory infiltrate, with a prominence of neutrophils and eosinophils
E. undifferentiated large epithelial cells with round vesicular nuclei and prominent nucleoli in a syncytial arrangement with a marked lymphocytic infiltration

Correct Answer: D
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Given the history of allergies and the finding of bilateral polypoid masses, it is most likely that this patient has nasal polyps, the typical histology of which is as

described. Hyperkeratotic squamous epithelium with a submucosal core of myxoid connective tissue, frequent blood vessels, mild fibrosis, and a mononuclear infiltrate (choice A) is the histological description of a vocal cord polyp. Myofibroblastic proliferation in a dense fibrovascular stroma with numerous endothelial-lined channels (choice B) describes the histology of a nasopharyngeal angiofibroma. Papillomatous proliferation of quamous epithelium extending downward through the submucosal connective tissue (choice C) refers to an inverted papilloma. An undifferentiated large epithelial cells with round vesicular nuclei and prominent nucleoli in a syncytial arrangement with a marked lymphocytic infiltration (choice E) is the histological description of an undifferentiated nasopharyngeal carcinoma.

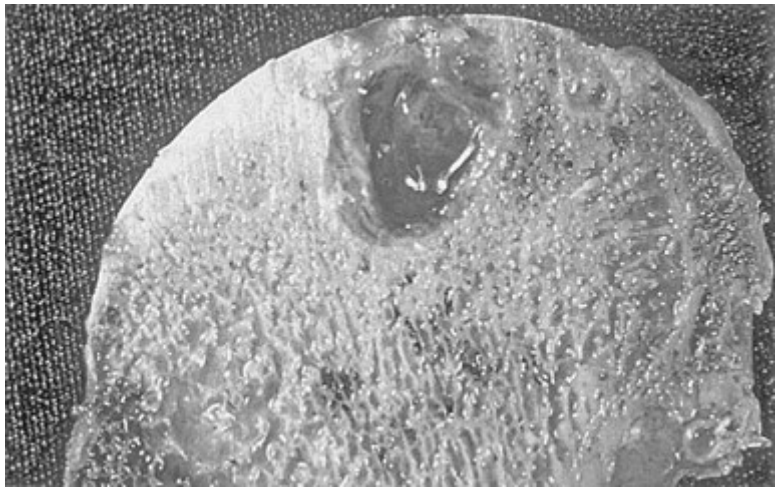
QUESTION 433
A 71-year-old woman suffers severe head injuries in a mugging and is hospitalized in a comatose state. While in the hospital, she develops severe pneumonia and on day 11 goes into cardiac arrest and cannot be resuscitated. At autopsy she is found to have advanced coronary atherosclerosis and a pulmonary embolism judged to have occurred within the past 23 days. The coroner should list which of the following on the death certificate as the underlying (or proximate) cause of death?

A. atherosclerosis
B. blunt trauma to the head GI
C. cardiopulmonary arrest
D. pneumonia
E. pulmonary embolism

Correct Answer: B
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
The proximate or underlying cause of death is the initiating event that led to the person's death and is what should be listed on the death certificate as the cause of death. In this case, if the woman had not been struck on the head she would not have been hospitalized, not contracted a nosocomial pneumonia (choice D), not had a pulmonary embolism due to the prolonged immobilization (choice E), and not had a cardiopulmonary arrest (choice C). Atherosclerosis (choice A) must have been present for many years prior to the mugging and had no role in her death.

QUESTION 434
A 66-year-old woman with a 3-year history of right hip pain undergoes a prosthetic hipreplacement. A photograph of her diseased femoral head is displayed in below figure. What is the likely cause of this abnormality?



A. benign neoplastic process
B. coagulopathy
C. degenerative process
D. infection
E. malignant neoplastic process

Correct Answer: C
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
The femoral head shows marked degenerative osteoarthritis. The gradual destruction of articular cartilage can eventually lead to joint compromise through eburnation, osteophyte formation, subchondral cysts, and osteochondral loose body formation. Clinically, these anatomic changes are reflected as joint pain and a restricted range of motion. Figure does not display evidence of a benign neoplasm (choice A), coagulopathy (choice B), infection (choice D), or malignant neoplastic process (choice E).

QUESTION 435
A 51-year-old alcoholic man is admitted to the emergency room with a 6-hour history of severe epigastric pain that radiates to his back and is more intense in a supine position. Physical examination reveals tachycardia, hypotension, and low-grade fever consistent with the early stage of shock. Which of the following serum measurements would be most useful in providing a diagnosis of his condition?

A. amylase

B. aspartate aminotransferase
C. bilirubin
D. calcium
E. troponin I

Correct Answer: A
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
The hallmark of acute pancreatitis is abdominal pain that is initially localized to the epigastrium and later becomes diffuse. It typically radiates to the back and is frequently more intense in the supine position. Other common symptoms and signs include nausea, vomiting, and tachycardia. If the pancreatitis is severe, hypotension can occur due to extravasation of blood and fluids into peritoneal (third) spaces and shock may ensue. Measurement of both amylase and lipase enzyme levels are useful in the diagnosis of acute pancreatitis. Amylase levels rise early in the course of the disease, while elevation of lipase levels may not occur until 24 hours after onset of illness. Although false positives and false negatives do occur, an elevated amylase level in conjunction with a consistent pattern of acute epigastric/abdominal pain is considered evidence of acute pancreatitis if other acute surgical conditions have been ruled out. Aspartate aminotransferase (choice B) is produced by a number of tissues and is increased in a variety of diseases; however, its greatest value is in liver function testing. Bilirubin (choice C) may be increased in an alcoholic but has no value in the diagnosis of acute pancreatitis. Calcium soap formation in the areas of fat necrosis may lead to a decrease in serum calcium (choice D) levels, but this is considered to be a nonspecific test. Troponin I (choice E) is now the preferred serum marker for the diagnosis of MI and has no role in the diagnosis of acute pancreatitis.

QUESTION 436
A 26-year-old woman complains of the acute onset of anuria, purpura, and mental confusion. Her peripheral blood film displays marked thrombocytopenia and abundant schistocytes. Laboratory studies reveal elevations of bilirubin, creatinine, and lactose dehydrogenase. A skin biopsy shows numerous intravascular thrombi within the dermal microvasculature. What is the most likely diagnosis?

A. acute idiopathic thrombocytopenia purpura
B. BernardSoulier syndrome
C. Glanzmann thrombasthenia
D. MayHegglin anomaly
E. thrombotic thrombocytopenic purpura

Correct Answer: E
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Thrombotic thrombocytopenic purpura is an acute microangiopathic hemolytic anemia. The clinical picture usually includes mental alterations, anuria, mucosal

bleeding, and purpura. An abnormal platelet-aggregating substance is the likely initiating event. Acute idiopathic thrombocytopenia (choice A) does not have a hemolytic component, lacks renal failure, and does not display thrombi in the skin biopsy. BernardSoulier syndrome (choice B) and Glanzmann thrombasthenia (choice C) are hereditary disorders of platelet aggregation. Clinical symptoms of a coagulopathy usually occur in infancy. MayHegglin anomaly (choice D) is an inherited condition with thrombocytopenia and morphologically abnormal WBCs. Hemolysis, acute onset, and mental aberrations do not typify this disorder.

QUESTION 437
A 58-year-old man has a 5-year history of progressively worsening heart failure. An autopsy limited to the heart reveals extensive replacement of the myocardium by an acellular eosinophilic material. This material is most likely to be which of the following?

A. amyloid
B. calcium salt deposition
C. cholesterol
D. myocyte fibrinoid necrosis
E. postinfarctive cicatrix

Correct Answer: A
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Amyloid is an acellular material that is eosinophilic. After Congo-red staining, there is apple-green dichroism when examined under polarized light microscopy. Calcium salts (choice B) tend to be deeply basophilic, not eosinophilic, with routine stains. Cholesterol deposits (choice C) tend to dissolve out of tissues with routine processing agents and only empty outlines of where the crystals once were are present remain. Myocyte fibrinoid necrosis (choice D) would be moderately cellular and eosinophilic. Congo-red dichroism is not evident. A postinfarctive cicatrix (choice E) also displays a relatively acellular eosinophilic morphology. Congo-red staining would not be dichroic, however.

QUESTION 438
A 29-year-old male AIDS patient presents with discrete and confluent white plaques adherent to the oral and pharyngeal mucosa. Microscopic examination of these plaques would most likely reveal which of he following?

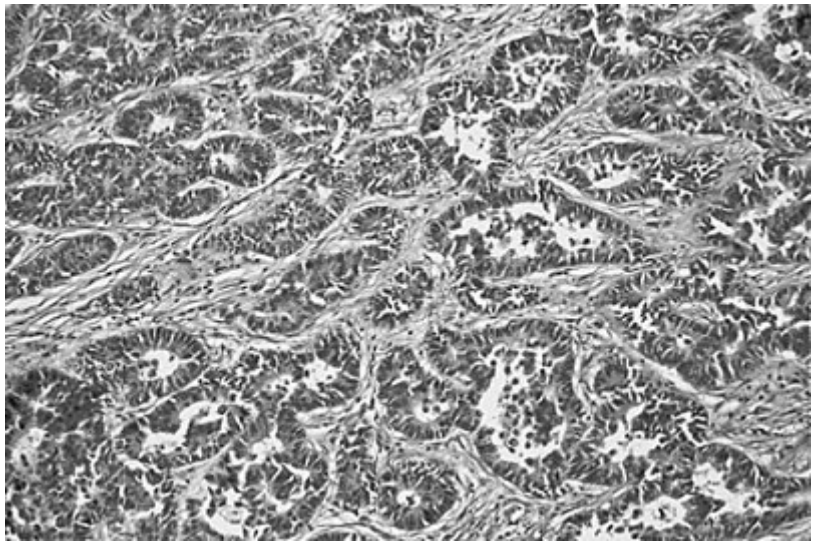
A. broad nonseptate mold with right angle branching
B. encapsulated yeast with narrow-based budding
C. narrow septate mold with acute angle branching
D. pseudohyphae with yeast-like forms
E. unencapsulated yeast with broad-based budding

Correct Answer: D
Section: Pathology and Path physiology

Explanation

Explanation/Reference:
Explanation:
Candida is the most common fungal infection in AIDS patients and most frequently involves the oral cavity and esophagus; the clinical appearance is typically as described. Microscopically, Candida is composed of pseudohyphae with some yeast-like forms. Choices A, B, C, and E are, respectively, the microscopic appearances of Mucor, Cryptococcus, Aspergillus, and Blastomyces.

QUESTION 439
A 67-year-old woman notices a lump in her left supraclavicular area. The lesion is excised and a section of it is shown in below figure. The microscopic appearance is most consistent with which of the following diagnoses?



A. adenocarcinoma
B. carcinoid
C. fibroadenoma
D. fibrosarcoma
E. malignant fibrous histiocytoma

Correct Answer: A
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
The finding of an enlarged left supraclavicular lymph node (Virchow or signal node) should raise the question of an underlying GI malignancy. This is confirmed in the above case by the microscopic findings in figure. The pleomorphism of these cells and the fact that they are located in a lymph node indicate that these are malignant cells. Additionally, the glandular appearance identifies this as an adenocarcinoma metastatic to a lymph node. Carcinoid tumors (choice B) arise from neuroendocrine cells present in the mucosa throughout the GI tract. About 40% are found in the appendix, where they are benign in 99% of cases. Another 25% are found in the ileum. Of these, about 60% are malignant. If they metastasize to the liver, they can give rise to the carcinoid syndrome. Fibroadenoma (choice C) is the most common benign tumor of the female breast. Fibrosarcoma (choice D) and malignant fibrous histiocytoma (choice E) are both fibroblastic sarcomas; the photomicrograph clearly indicates a malignancy of epithelial (glandular) origin.

QUESTION 440
A 56-year-old woman returns to clinic for a follow-up after undergoing a lung biopsy of a 1.4 × 2.1 cm, left upper lobe lesion originally discovered on chest x-ray. Her physician checks her record for the pathology report and reads that histology of the biopsy demonstrated "scattered spindle cells with a minimal mononuclear inflammatory infiltrate and few blood vessels in a background of abundant pale connective tissue. Small areas of calcification are observed and there is no evidence of normal lung parenchyma." Which of the following is most likely responsible for these findings?

A. deposition of amyloid protein
B. hamartoma formation
C. healing of an abscess
D. malignant transformation of type 1 pneumocytes
E. unresolved infection with Mycobacterium tuberculosis

Correct Answer: C
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
The first sentence of the pathology report describes the histological morphology of granulation tissue, representing evidence of healing within the biopsied lesion. The absence of normal lung parenchyma indicates that injury to the lung was extensive enough to prohibit regeneration, and this would be expected due to the liquefactive necrosis occurring with abscess formation. Areas of calcification can develop in any necrotic tissue and represent a nonspecific finding. Deposition of amyloid protein (choice A), or amyloidosis, is associated with particular chronic diseases (AA protein) or certain immunoglobulin-secreting neoplasms (AL protein). It appears histologically as extracellular, diffusely distributed, acellular material and is best demonstrated using Congo-red stain. The pathology report was not consistent with the morphology of a hamartoma (choice B), which refers to a disorganized mass of mature tissue indigenous to the organ in which it arises. There was also no cytological description suggestive of malignancy (choice D, malignant transformation of type 1 pneumocytes), such as pleomorphism or hyperchromatism. Granulation tissue could potentially be seen in an unresolved infection with M. tuberculosis (choice E); however, evidence of granuloma formation is necessary to establish the diagnosis.

QUESTION 441
Aliver biopsy of a 61-year-old man reveals the presence of clusters of cells with large, intracellular vacuoles and nuclei eccentrically displaced to the cell periphery.

From which of the following conditions does this patient most likely suffer?

A. alcoholism
B. chronic liver congestion
C. hepatitis A
D. metastatic colon carcinoma
E. portal vein thrombosis

Correct Answer: A
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
The biopsy findings are descriptive of macrovesicular fatty change, a characteristic morphological change in the liver of patients with alcohol abuse. Morphological changes in chronic liver congestion (choice B) would demonstrate areas of centrilobular necrosis and hemorrhage, with hemosiderin-laden macrophages and varying degrees of acute inflammation. Fatty change is unusual in hepatitis A (choice C), and in most forms of hepatitis overall with the possible exception of hepatitis C, where typical morphological changes would include cellular edema, a cytoplasmic ground glass appearance, lymphocytic infiltrate, and focal or centrizonal necrosis. Histological findings for metastatic colon carcinoma (choice D) would demonstrate pleomorphic cells with hyperchromatic nuclei, and possible mitotic figures. Liver biopsy of an area with portal vein thrombosis (choice E) would reveal sinusoidal distention with areas of hemorrhage and hepatocellular atrophy.

QUESTION 442
A 22-year-old man recovers from a bout of hepatitis Aafter 3 weeks. One year after this infection, which of the following would a liver biopsy most likely demonstrate?

A. bridging fibrosis
B. lymphocytes spilling out of the portal tracts with piecemeal necrosis
C. lymphocytic infiltrates limited to portal triads
D. massive hepatic necrosis
E. normal histology

Correct Answer: E
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Hepatitis A does not progress to a chronic phase so one year after infection the liver histology will appear as normal. The other choices are found in active hepatitis.

Bridging fibrosis (choice A) and lymphocytes spilling out of the portal tracts with piecemeal necrosis (choice B) are major features of chronic hepatitis although both can be found in severe acute hepatitis. Lymphocytic infiltrates limited to portal triads (choice C) may be seen in mild acute or chronic hepatitis. Massive hepatic necrosis (choice D) is associated with fulminant hepatitis but can also be caused by various chemical and drug toxicities.

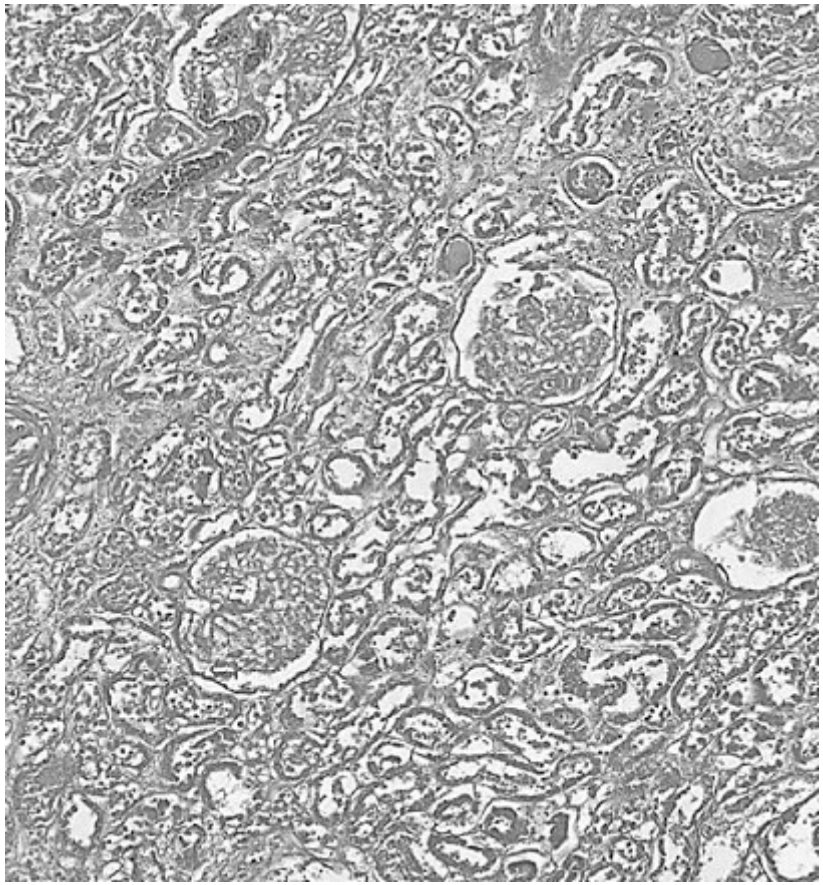
QUESTION 443
A 27-year-old woman who recently delivered her first child develops an infiltrative mass in the anterior abdominal wall. A biopsy reveals sweeping fascicles of well-differentiated, plump monomorphic fibroblasts that infiltrate surrounding tissues. Based on this information, what is the most likely diagnosis?

A. desmoid tumor
B. fibrosarcoma
C. malignant fibrous histiocytoma
D. myositis ossificans
E. nodular fasciitis

Correct Answer: A
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Desmoid tumors are mesenchymal tumors that are locally aggressive but do not metastasize and have a benign microscopic appearance characterized by well-differentiated fibroblasts. Those tumors arising in the anterior abdominal wall are usually seen in women who are pregnant or recently postpartum. Fibrosarcomas (choice B) are rare malignant mesenchymal tumors that can metastasize and would typically be expected to have a more pleomorphic microscopic appearance (often with a "herringbone pattern") than that seen in desmoid tumors. Malignant fibrous histiocytomas (choice C) are also malignant mesenchymal tumors that would have a pleomorphic microscopic appearance. Myositis ossificans (choice D) is a non-neoplastic lesion that often forms following blunt trauma to muscle in a lower limb. The initial hematoma undergoes organization with calcification and can have a pleomorphic appearance with numerous mitoses, leading to the possibility of a misdiagnosis as a malignancy. Of special note, however, is that the bone in myositis ossificans matures from the periphery to the center, whereas the opposite pattern is seen in a malignant tumor. Nodular fasciitis (choice E) presents as a rapidly growing, potentially painful mass that may occur in association with prior trauma. Its histological appearance can be worrisome and, similar to myositis ossificans, may lead to misdiagnosis as a malignancy (sarcoma) as it is somewhat pleomorphic with immature fibroblasts and many mitoses. However, these lesions are self-limited and excision is curative.

QUESTION 444
A 72-year-old woman was hospitalized after becoming acutely ill. Despite intervention, she died 9 days later. One of the findings at her autopsy is shown in below figure which is a section of her left kidney. Which of the following conditions could have led to the changes seen in this patient's kidney and was most likely the reason for her hospitalization?



A. MI
B. pyelonephritis
C. renal carcinoma
D. sepsis
E. shock

Correct Answer: A
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
The photomicrograph in figure shows recognizable glomeruli and tubules but no nuclear staining, enabling one to recognize this as a renal infarct. Most renal infarcts result from thromboemboli originating in the left ventricle of a patient who has had an MI. This woman's age and her history of an acute illness leading to her death 9 days later are compatible with this sequence of events. The histology of pyelonephritis (choice B) would show viable kidney involved in an inflammatory response. Additional findings would depend upon whether it is an acute or chronic pyelonephritis. Renal carcinoma (choice C) would show viable malignant cells and not necrotic normal renal tissue. Sepsis choice D) may show indications of the infection within the renal parenchyma with an associated inflammatory response, but this is not seen in the image. Shock (choice E) is associated with acute tubular necrosis, which is a patchy necrosis affecting the proximal more than the distal tubules, but the glomeruli remain unaffected. The image shows complete necrosis of all renal elements.

QUESTION 445
A 31-year-old previously healthy woman develops pelvic inflammatory disease and subsequently undergoes a complete hysterectomy; her ovaries are left intact. Incidental findings in the myometrium are three discrete, sharply circumscribed masses that range from 4 to 8 cm in diameter and have a whitish, whorled cut surface. What would have been the most likely outcome over the next 5 years if these masses had not been removed?

A. complete regression
B. continued expansile growth
C. infiltration into surrounding tissues
D. metastasis via blood vessels
E. necrosis and hemorrhage

Correct Answer: B
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
This description of the myometrial masses is consistent with leiomyomas, benign tumors of smooth muscle origin. Uterine leiomyomas are the most frequent tumor in women and are estimated to occur in up to 75% of women of reproductive age. As benign tumors, the expected outcome for such masses in a premenopausal woman would be continued expansile growth. Growth of leiomyomas is stimulated (but not initiated by) estrogen, therefore, regression (choice A) would be more probable in a woman of postmenopausal age or a younger woman who may have had her ovaries removed but is unlikely to be complete. Infiltration into surrounding tissues (choice C) and metastasis via blood vessels (choice D) are characteristics of malignant tumors only. While necrosis and hemorrhage (choice E) may rarely occur in benign neoplasms, they are quite characteristic of malignant neoplasms, as blood vessels are more numerous and are often poorly formed. Uterine leiomyomas and colonic adenomas are two of the exceptions to the general rule that benign neoplasms develop as single lesions.

QUESTION 446
A 47-year-old man has undergone a gradual personality change over the past 67 months with increasing moodiness and irritability During your examination you note some choreiform involuntary movements and also recognize some cognitive impairment. Afterward you talk to the man's brother who accompanied the patient to your office and he tells you that their father had similar problems for about a year prior to his death. If you could examine this patient's brain, which of the following would you expect to find?

A. areas of demyelination of the white matter
B. atrophy and loss of neurons of the caudate nucleus
C. loss of pigmented neurons of the substantia nigra
D. neurons ballooned with cytoplasmic vacuoles
E. selective atrophy of anterior frontal and temporal lobes

Correct Answer: B
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
In Huntington's disease there is a symmetric atrophy of the caudate nuclei with a great reduction in the number of neurons. The putamen is also affected but usually less so. Areas of demyelination of white matter (choice A) are the classic finding in multiple sclerosis. Loss of pigmented neurons of the substantia nigra (choice C) is a consistent change seen in Parkinson's disease. Neurons ballooned with cytoplasmic vacuoles (choice D) may be seen in a number of lysosomal storage diseases of which Tay- Sachs disease is the classic example. Selective atrophy of anterior, frontal, and temporal lobes (choice E) is seen in Pick disease. There is a severe atrophy of the frontal and temporal lobes which can be sufficient to produce the "knife-edge" appearance characteristic of this disease.

QUESTION 447
A 54-year-old construction worker collapses at his work site and is brought to the emergencyroom in a comatose state. His skin is dry and hot and his rectal temperature is 105℉. Which of the following is the most likely diagnosis?

A. heat cramps
B. heat exhaustion
C. heat stroke
D. malignant hyperthermia
E. pyrexia

Correct Answer: C
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Heat stroke is a life-threatening condition resulting from a failure of heat regulation. It is marked by high body core temperature and the failure of sweating. Heat cramps (choice A) are the result of the loss of fluid and electrolytes through sweating. Painful cramping of muscles can occur, but core temperature remains normal. Heat exhaustion (choice B) results from excessive sweating and failure to replace the lost fluid. This results in hypovolemia, venous pooling, and reduced cardiac output. The skin is wet and the temperature is usually normal. Heat exhaustion is not life threatening, and there is usually spontaneous recovery when the person is moved to a cool place. Malignant hyperthermia (choice D) is an inherited condition in which there is an increased temperature when the person is

exposed to certain anesthetics. It has no relationship to environmental temperature. Pyrexia (choice E) is fever and is usually defined as a cytokine-mediated increase in body temperature as part of a response to disease. This results in the hypothalamus having a higher "set point" for the body's temperature.

QUESTION 448
A 38-year-old woman with a history of 35 urinary tract infections over the past 2 years presents with another similar episode, including symptoms of dysuria and flank pain. Additional history includes one episode of a renal stone. Renal ultrasound is unremarkable. Urinalysis reveals pyuria, no RBCs, and no casts. Urine culture is positive for E. coli. Which of the following is the most likely underlying cause of this patient's urinary tract infections?

A. autosomal dominant polycystic kidney disease
B. focal segmental glomerulosclerosis
C. medullary sponge kidney (MSK)
D. minimal change disease
E. renal cell carcinoma

Correct Answer: C
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
MSK is a relatively common disorder, appearing on approximately 1% of all intravenous pyelograms. It is a congenital, typically bilateral condition and almost all cases are sporadic. The pathological lesion consists of multiple cystic dilations of the medullary collecting ducts. Patients are generally asymptomatic until their third or fourth decade when secondary complications of urinary tract infections (UTIs), calculi, or hematuria may develop. The condition is usually benign and renal function is generally normal; in atypical cases, renal damage may result from secondary pyelonephritis or severe stone disease. Although UTIs and calculi may be complications of autosomal dominant polycystic kidney disease (choice A), this genetic condition is much more severe than MSK and chronic renal failure is the typical outcome. Patients usually present with many other common features, including hematuria, proteinuria, and hypertension; renal ultrasound is capable of detecting cystic disease in virtually all patients over the age of 30. Focal segmental glomerulosclerosis (choice B) typically presents as nephrotic syndrome or subnephrotic proteinuria, accompanied by hypertension and mild renal insufficiency in some cases. This disease may occur idiopathically or as a secondary manifestation of other conditions (e.g., HIV). There is no association with UTIs and diagnosis is made by biopsy. Minimal change disease (choice D) (also nil disease, lipoid nephrosis) is the leading cause of nephrotic syndrome in children. While adults may be affected, peak incidence of disease is 28 years. The distinguishing pathology is diffuse effacement of foot processes of glomerular visceral epithelial cells. Diagnosis is made by biopsy and electron microscopy analysis as glomeruli appear essentially normal on light microscopy, which is a disease-defining characteristic. Etiology is unknown although an immune dysfunction has been proposed. Increased incidence of disease in adults with lymphoproliferative malignancies has been reported. Disease is often limited to massive proteinuria and prognosis is excellent; response to corticosteroid therapy is dramatic. Renal cell carcinoma (also clear cell carcinoma) (choice E) is most common in older individuals (>60), and patients often present with symptoms of hematuria and flank pain; constitutional symptoms of cancer (e.g., fever, fatigue, weight loss) may also be reported. Additional findings may develop from any of a number of paraneoplastic syndromes connected with this malignancy; there is no association with recurrent UTIs however. CT scan is used for standard evaluation, although ultrasound is capable of detecting most lesions.

QUESTION 449
A 45-year-old woman complains of gradually increasing fatigue. On physical examination she is noted to have obesity, hypertension, buffalo hump deformity of her back, moon facies, abdominal striae, and muscle weakness. Radiographic imaging studies identify an abnormality of her right adrenal gland which is then surgically

resected. The intact specimen weighed 24 g. A hemisection of the gland is displayed in below figure. What is the most likely diagnosis?

A. adrenal cortical adenoma
B. Krukenberg tumor
C. multifocal infarction
D. neuroblastoma
E. pheochromocytoma

Correct Answer: A
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
The adrenal gland shown in figure contains a cortical adenoma. Grossly, these neoplasms appear as well-demarcated, round to oval, yellowish, solitary nodules arising within the adrenal cortex. The surrounding nonneoplastic cortex is thinned and atrophic. The underlying medulla is normal. The associated clinical findings suggest Cushing syndrome due to excessive secretion of cortisol by the adenoma. Krukenberg tumor (choice B) is an enlarged ovary due to metastatic carcinoma. Adrenal infarcts (choice C) may be associated with certain bacterial infections and shock. The gland appears diffusely hemorrhagic and necrotic, without the formation of a discrete tumor nodule. Neuroblastoma (choice D) is an adrenal tumor of infancy. The typical gross appearance is a large, tan hemorrhagic mass. Hypercortisolemia is not seen. Apheochromocytoma (choice E) appears as a hemorrhagic, red- tan medullary tumor. Clinically, there may be signs of excessive norepinephrine secretion.

QUESTION 450
A 74-year-old man dies after a 4-day hospital course with a clinical diagnosis of adult respiratory distress syndrome. At autopsy a pathologic diagnosis of diffuse alveolar damage is rendered. Which of the following microscopic findings of the lung tissue is most expected at autopsy?

A. alveolar hyaline membrane formation
B. eosinophilic inflammatory infiltrates
C. hemorrhagic infarction
D. pleural effusion and fibrous pleuritis
E. pulmonary vasculature occluded by microthrombi

Correct Answer: A
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Hyaline membranes are usually seen microscopically in lungs showing diffuse alveolar damage. Grossly, the lungs are heavy, wet, and meaty. The clinical course is termed adult respiratory distress syndrome and is characterized by relative unresponsiveness to oxygen therapy. Eosinophilic inflammatory infiltrates (choice B), hemorrhagic infarction (choice C), pleural effusions (choice D), and vascular microthrombi (choice E) are not typically seen with diffuse alveolar damage.

QUESTION 451
A 35-year-old lifeguard requests a consultation for a lesion on his upper back that his girlfriend first noticed about a year ago. He states that he is more concerned since it has increased in size. Your examination reveals a 15 × 16 mm raised nodule with irregular borders and variable areas of dark and light pigmentation. This most likely represents which of the following?

A. actinic keratosis
B. compound nevus
C. Lentigo simplex
D. malignant melanoma
E. seborrheic keratosis

Correct Answer: D
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Askin lesion that is >10 mm, increasing in size, has variable pigmentation, and irregular borders elicits extreme concern and is most probably a malignant

melanoma. Actinic keratoses (choice A) are potentially premalignant skin lesions that, as the name suggests, are the result of chronic sun exposure; they are typically <1 cm in diameter. The accumulation of keratin on the surface imparts a rough or scaly texture to the skin. Compound nevi (choice B) (moles) develop when nests of nevi cells (modified melanocytes) extend from the dermoepidermal junction (junction nevus) into the underlying dermis; they are typically brown or flesh-colored, raised, dome-shaped lesions that are symmetrical and uniform. Lentigo simplex (choice C) refers to a benign focal hyperplasia of melanocytes; lesions typically appear as small (<1 cm) brown, sharply defined, oval macules. They have no predisposition to neoplastic change. Seborrheic keratoses (choice E) are benign pigmented skin tumors that are usually found on older individuals; lesions are flat, round waxy plaques that may seem to be glued on to the skin. Close inspection reveals pore-like structures with keratin plugs which helps to differentiate them from melanomas. These lesions have no malignant potential, but the sudden appearance of multiple lesions could be a paraneoplastic syndrome indicating a visceral malignancy (sign of Leser-Trélat).

QUESTION 452
A 45-year-old man is bitten by a poisonous snake the venom of which triggers the release of thromboplastin in his circulation. Which of the following would you most expect to see as a consequence of this event?

A. abnormal neutrophilic degranulation resulting in small vessel vasculitis and subsequent hemorrhage or thrombosis
B. deposition of antigen-antibody complexes in various tissue beds, causing vasculitis with thrombosis, glomerulonephritis, and arthritis
C. formation of multiple, migratory peripheral venous thromboses without evidence of tissue ischemia or hemorrhage
D. immediate mast cell degranulation of vasoactive amines followed by progressive vascular leakage and subsequent tissue ischemia
E. widespread development of thrombi in the microvasculature followed by hemorrhage

Correct Answer: E
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Thromboplastin-like substances (or tissue factor) released into the circulation can initiate disseminated intravascular coagulation (DIC). In this situation, thromboplastin activates the coagulation cascade, leading to the formation of multiple thrombi distributed throughout the microvasculature. As this process progresses, platelets and coagulation factors are consumed and hemorrhage can occur; bleeding is exacerbated by activation of the fibrinolytic system. Abnormal neutrophilic degranulation resulting in small vessel vasculitis and subsequent hemorrhage or thrombosis (choice A) is an example of a type II hypersensitivity reaction associated with circulating antineutrophil cytoplasmic antibodies (ANCA); examples of ANCA-associated vasculitides include Wegener granulomatosis and Churg-Strauss syndrome. Deposition of antigen-antibody complexes in various tissue beds, causing vasculitis with thrombosis, glomerulonephritis, and arthritis (choice B) describes a nonspecific systemic type III hypersensitivity response (which takes several days to develop). Formation of multiple, migratory peripheral venous thromboses without evidence of tissue ischemia or hemorrhage (choice C) refers to igratory thrombophlebitis, a condition associated with certain types of cancers, particularly adenocarcinomas in which hypercoagulability occurs as a paraneoplastic syndrome; this is referred to as Trousseau syndrome. These and other tumors are also independently capable of initiating DIC. Immediate mast cell degranulation of vasoactive amines followed by progressive vascular leakage and subsequent tissue ischemia (choice D) describes anaphylaxis, a type I hypersensitivity reaction.

QUESTION 453
A 36-year-old man is now in his third year of steroid therapy since being diagnosed with a systemic vasculitis. Prior to initiating treatment in the acute phase of the disorder, he underwent a biopsy of a medium-sized artery. This biopsy specimen displayed fibrinoid necrosis of the media accompanied by a transmural acute inflammatory infiltrate. Significant negative clinical findings included a normal aortic arch, absence of giant cells in the artery biopsy, normal upper airway

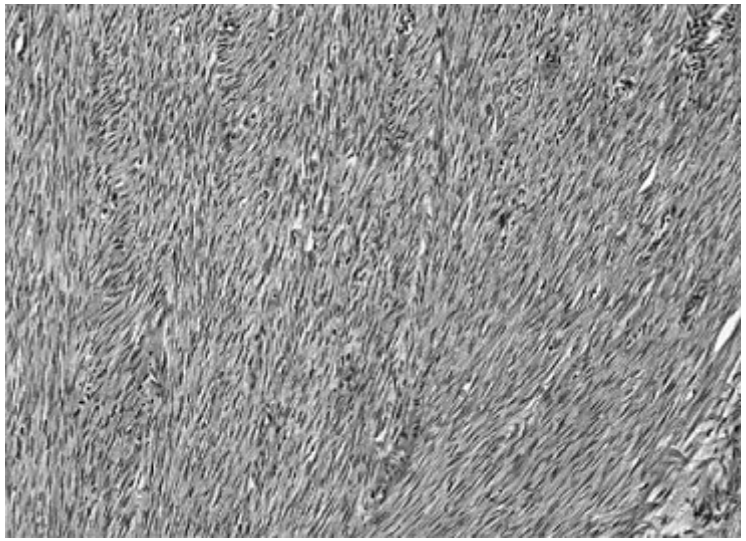
examination, and no history of tobacco use. Which of the following disorders best correlates with these findings?

A. Kawasaki disease
B. polyarteritis nodosa
C. Takayasu disease
D. temporal arteritis
E. thromboangiitis obliterans

Correct Answer: B
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Polyarteritis nodosa is a systemic vasculitis primarily seen in young adult males. Fibrinoid necrosis and acute inflammation are seen microscopically in the acute phase. Mucocutaneous lymph node syndrome (Kawasaki disease) (choice A) is a childhood disorder with coronary vasculitis, cervical lymphadenopathy, and acute onset. Takayasu disease (choice C) is characterized by fibrosis of the upper aorta. The classic patient is a Japanese woman with HLA-DR4. Temporal or giant cell arteritis (choice D) is a granulomatous arterial inflammation seen in the elderly. The superficial temporal and intercranial arteries are preferentially involved. Thromboangiitis obliterans (choice E) is an occlusive disease of small arteries strongly related to cigarette smoking

QUESTION 454
A 34-year-old woman has a history of menorrhagia. Within the wall of her uterus are several solid nodules of various sizes. The histological appearance of one of the nodules is depicted in below figure.
These nodules represent which of the following?



A. adenomyosis
B. Krukenberg tumors
C. leiomyomas
D. metastatic malignancy
E. Ovarian ectopias

Correct Answer: C
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Figure displays interweaving bundles of smooth muscle cells, which, as a discrete myometrial nodule, define a leiomyoma. These are common tumors that may be asymptomatic or produce menorrhagia. Gross appearance is that of a solid white nodule. Adenomyosis (choice A) may clinically and grossly mimic leiomyomas. Adenomyosis, however, has a triphasic microscopic appearance consisting of benign endometrial glands, benign endometrial stroma, and smooth muscle hypertrophy. AKrukenberg tumor (choice B) is replacement of the ovary by metastatic GI adenocarcinoma. The diagnosis of metastatic malignancy (choice D) is not supported by the photomicrograph of a benign process. Ovarian ectopia (choice E) is exceedingly rare and is incompatible with the histology of the photomicrograph.

QUESTION 455
A 73-year-old man with a history of an MI 2 years ago has been experiencing gradually increasing shortness of breath over the past 4 weeks. Physical examination reveals bilateral crackles on pulmonary auscultation and 2+ pitting edema of the lower legs bilaterally. Which of the following most likely occurred in this patient to

produce these changes?

A. interventricular septal wall thickening
B. lobar pneumonia
C. new MI
D. spontaneous idiopathic pneumothorax
E. ventricular aneurysm rupture

Correct Answer: C
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Bilateral crackles on lung auscultation and 2+ pitting edema of the bilateral lower extremities are signs of left-sided and right-sided congestive heart failure, respectively. The only logical choice that could lead to both in this patient is an MI, where left ventricular failure subsequently leads to right ventricular failure. Interventricular septal wall thickening (choice A) is a particular characteristic of idiopathic hypertrophic cardiomyopathy, and frequently causes outflow tract obstruction during systole. It is an autosomal-dominant genetic disease leading to serious progressive cardiac abnormalities typically beginning in young adulthood, and is a common cause of sudden, otherwise unexplainable, death in young athletes. While lobar pneumonia (choice B) is common in older patients, and could lead to shortness of breath, it would not be associated with right heart failure and bilateral lower extremity edema. Similarly, a spontaneous idiopathic pneumothorax (choice D) may also result in shortness of breath, but does not cause right heart failure; this phenomenon is most commonly encountered in young individuals, not an older population. Ventricular aneurysms (choice E) occur as a possible complication of extensive transmural anteroseptal MIs in which a large area of thin scar tissue produces external bulging; they are not associated with rupture.

QUESTION 456
A 28-year-old woman has an ultrasound examination during the second trimester of her third pregnancy. She is found to have greatly decreased amniotic fluid but the fetus appears to be the appropriate size for the gestational age. Her two previous pregnancies produced normal-term infants. The family history is otherwise unremarkable. Which of the following conditions most likely explains these findings?

A. bilateral cystic renal dysplasia
B. bronchopulmonary dysplasia
C. hypoplasia of the lungs
D. Klinefelter syndrome
E. placenta previa

Correct Answer: A
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Most of the amniotic fluid is derived from the urine of the fetus. In a fetus with bilateral cystic renal dysplasia, little or no urine is being produced, which leads to the oligohydramnios seen in this case. Bronchopulmonary dysplasia (choice B) may be seen in babies who have respiratory distress syndrome and are given oxygen therapy. Hypoplasia of the lungs (choice C) is a consequence of oligohydramnios because inhalation of amniotic fluid by the fetus is necessary for normal lung development. Klinefelter syndrome (choice D) occurs in males with XXY karyotype and does not explain the findings in this case. Placenta previa (choice E) occurs when there is abnormally low implantation of the fertilized ovum in the uterus such that it overlies the internal os.

QUESTION 457
A2-month-old girl with a history of persistent physiologic jaundice following birth is now reported by her parents to sleep excessively and display little activity. Physical examination reveals abnormal deep tendon reflexes, hypothermia, and muscular hypotonia. Based on this information, which of the following would be the best therapy for her condition?

A. antibiotics
B. growth hormone
C. thiamine
D. thyroxine
E. vitamin D

Correct Answer: D
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
This infant has cretinism, a condition caused by a neonatal lack of thyroxine. Thyroid agenesis, iodine deficiency, ingestion of goitrogens, and hereditary enzymatic deficiencies may all result in a relative lack of biologically active thyroxine. Affected children may display lethargy, jaundice, hypothermia, muscular hypotonia, and mental retardation. Medicinal replacement of thyroxine is therapeutic. The mental retardation may not be reversible, however, unless treated early. Antibiotics (choice A) have no effect in treating cretinism. Growth hormone (choice B) is an effective treatment for pituitary dwarfism but it has no benefit in cretinism. Treatment with thiamine (choice C) is the appropriate therapy for beriberi, not cretinism. A lack of vitamin D (choice E) causes rickets, not cretinism.

QUESTION 458
On otoscopic examination, a patient is found to have a 2-cm mass protruding from a retraction pocket in his right tympanic membrane. The lesion is removed and determined to be a cystic mass lined by squamous epithelium containing desquamated cellular debris and a mononuclear infiltrate. Which of the following is the most likely cause of this lesion?

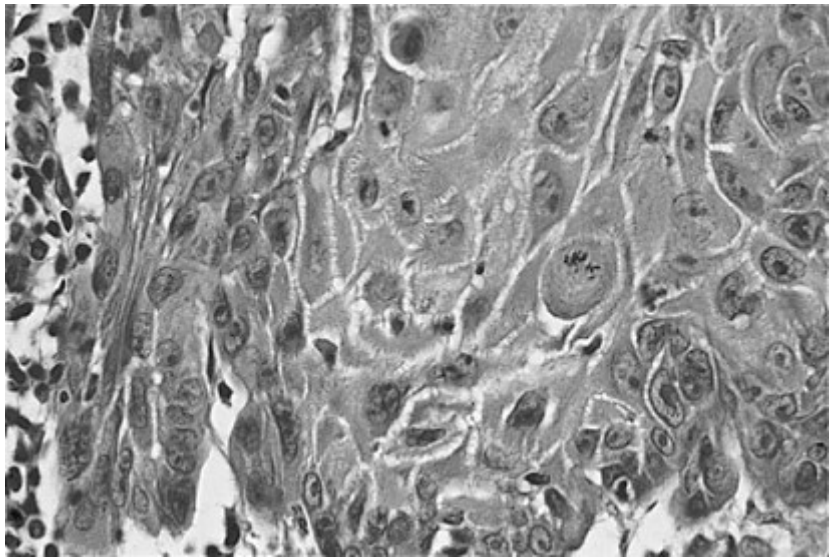
A. barotraumas
B. chronic otitis media
C. exostosis formation in the external auditory canal
D. squamous cell carcinoma of the external auditory canal

E. tympanosclerosis

Correct Answer: B
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
A cholesteatoma is a cystic lesion lined by squamous epithelium and containing keratinaceous material. It is most probably formed by the protrusion of squamous epithelium from the middle ear canal through a perforation in the eardrum that was itself the result of chronic otitis media. Barotrauma (choice A) to the ear can be produced by sudden changes in atmospheric pressure compared to the relatively low middle ear pressure. This results in inflammation of the mucous membrane of the middle ear (serous otitis media). Exostosis formation in the external auditory canal (choice C) refers to the growth of a bony swelling that may occur with chronic exposure to cold water. Squamous cell carcinomas of the external auditory canal (choice D) are unusual and have a histological appearance similar to other squamous cell carcinomas (polygonal cells with prickles and pearls), which is quite different from the description given. Tympanosclerosis (choice E) of the tympanic membrane results from resolved acute otitis media producing acellular hyaline and calcific deposits in the tympanic membrane.

QUESTION 459
A 66-year-old man presents with a 3-month history of intermittent dysphagia that has now become constant and is accompanied by pain and some weight loss. X-rays of the esophagus with barium swallow show structural and filling defects, and reduced peristalsis. Abiopsy is taken and is shown in below figure. The best diagnosis is which of the following?



A. adenocarcinoma of the esophagus

B. Barrett esophagus
C. Candida esophagitis
D. fibrous stricture of the esophagus
E. squamous cell carcinoma of the esophagus

Correct Answer: E
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
The cells in figure are pleomorphic and invasive indicating their malignant character. Additionally, there are many intercellular bridges ("prickles") joining the cells indicating their squamous origin. Therefore, this is a squamous cell carcinoma. The presentation described is fairly typical for squamous cell carcinoma of the esophagus. Its development is closely associated with the risk factors of smoking and alcoholism. Adenocarcinoma of the esophagus (choice A) arises in the lower esophagus in a background of Barrett esophagus and is, of course, composed of malignant glandular cells, not the squamous cells seen here. Barrett esophagus (choice B) demonstrates metaplastic glandular epithelium. Candida esophagitis (choice C) is recognized by the presence of yeast and pseudohyphae. Fibrous stricture (choice D) can be caused, for example, by severe chronic reflux from ingestion of corrosives and produces fibrosis. Lye ingestion is associated with a 1000-fold increase in risk for squamous cell carcinoma.

QUESTION 460
During a routine physical examination, a 16-year-old boy is found to have only minimal secondary sexual development, gynecomastia, and a tall, eunuchoid habitus. Achromosomal determination on this individual would most likely reveal which of the following?

A. 45, XO
B. 45, YO
C. 46, XX
D. 46, XY
E. 47, XXY
F. 47, XYY

Correct Answer: E
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
The physical description of this boy is that of Kleinfelter syndrome. This condition is not usually diagnosed until after puberty when the secondary sexual characteristics do not develop normally. Most of these individuals are 47, XXY but some may have additional X or Y chromosomes. 45, XO (choice A) is characteristic of a female with Turner syndrome which is usually diagnosed early in life. 45, YO (choice B) is not compatible with life and is not seen. 46, XX (choice

C) is the chromosome number of a normal female and 46, XY (choice D) is that of a normal male. Males with 47, XYY (choice F) are above average in height and have an increased incidence of developing severe acne. IQ is normal but there may be mild learning disabilities.

QUESTION 461
A 75-year-old woman, a life-long smoker with Type II diabetes, dies secondary to complications of alcoholic cirrhosis. At autopsy, a hard, infiltrative mass is observed in the head of the pancreas. Microscopic examination of the body and tail of the pancreas demonstrates acinar loss with marked fibrosis, duct dilation, some lymphocytic infiltration, and sparing of islets. Based upon the information given, which of the following would most likely represent the microscopic appearance of the pancreatic mass?

A. deposition of an acellular, eosinophilic material between parenchymal cells
B. diffuse interstitial fibrosis with intraand extracellular golden-brown pigment
C. moderately differentiated, mucussecreting cells in a dense, fibrotic stroma
D. necrosis of pancreatic parenchyma and adjacent fat with a neutrophil infiltrate
E. plugging of ducts, atrophy of exocrine glands, and fibrosis

Correct Answer: C
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Little is known about the etiology of pancreatic adenocarcinoma although smoking, chronic pancreatitis, and diabetes mellitus (especially in women) have been associated with an increased risk for the disease. The microscopic description for the body and tail of the pancreas is consistent with chronic pancreatitis, thus, this woman had all three of these risk factors. The microscopic appearance of ductal pancreatic adenocarcinoma most usually (~70%) demonstrates moderately to well-differentiated cells producing mucus and surrounded by a dense fibrotic stroma. Deposition of an acellular, eosinophilic material (choice A) is a description of amyloidosis. Diffuse interstitial fibrosis with intra- and extracellular golden-brown pigment (choice B) describes hemochromatosis. Necrosis of pancreatic parenchyma and adjacent fat with inflammation (choice D) would be seen in acute pancreatitis. Plugging of ducts, atrophy of exocrine glands and fibrosis (choice E) may be seen in cystic fibrosis. In addition, choices A, B, D, and E would not be expected to be associated with a focal mass.

QUESTION 462
A 6-year-old child has a long history of a hereditary bleeding disorder characterized by spontaneous nontraumatic hemorrhages into joint spaces, skeletal muscle, and mucous membranes. Laboratory studies reveal a normal prothrombin time, elevated partial thromboplastin time, very low factor VIII, normal factor X, normal factor XI, and normal platelet aggregation studies with ristocetin. Which of the following is the most likely diagnosis?

A. Christmas disease
B. hemophilia A
C. hemophilia B
D. Rosenthal syndrome
E. von Willebrand disease

Correct Answer: B
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Hemophilia A is a genetic disorder characterized by very low levels of factor VIII, elevated partial thromboplastin time, normal prothrombin time, normal platelet aggregation with ristocetin, and spontaneous hemorrhages into joints, soft tissues, and mucosal surfaces. Christmas disease (choice A) is an alternative term for hemophilia B. Hemophilia B (choice C) is a hereditary coagulopathy due to a very low level of factor IX. Rosenthal syndrome (choice D) defines a deficiency of factor XI. von Willebrand disease (choice E) is characterized by a mild hereditary bleeding diathesis and abnormal platelet aggregation with ristocetin.

QUESTION 463
A 15-month-old baby girl is brought to the emergency room by her parents for a 1-week history of malaise, poor feeding, mild fever, and diarrhea. Physical examination is unremarkable. This is the sixth such occasion for which the parents have brought their daughter to a physician. Past visits have revealed repeated infections, including Candida, cytomegalovirus, and M. avium-intracellulare. A complete blood count (CBC) is remarkable only for a low total lymphocyte count. Immunoglobulin levels are normal. Alymph node biopsy is remarkable for paracortical cell depletion, but is otherwise normal. Which of the following is the most likely diagnosis?

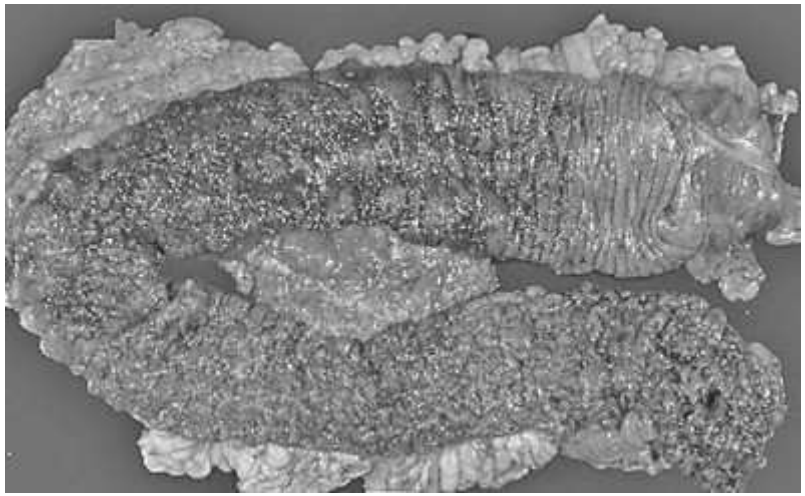
A. Bruton congenital agammaglobulinemia
B. chronic granulomatous disease of childhood
C. severe combined immunodeficiency disease
D. thymic hypoplasia
E. Wiskott-Aldrich syndrome

Correct Answer: D
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
In thymic hypoplasia, the congenital developmental failure of the thymus leads to a lack of T- lymphocytes in the blood as well as in appropriate areas of lymph nodes (paracortical area). Deficient T-cell immunity will thus lead to severe, recurrent viral, mycobacterial, fungal, or protozoal infections during infancy. Thymic hypoplasia is best described in association with DiGeorge syndrome, in which defective embryological development of the third and fourth pharyngeal pouches results in developmental failure of thymus and parathyroid formation, congenital heart defects, and severe hypocalcemia, secondary to hyperparathyroidism. An associated, but less well-defined, entity is Nezelof syndrome, in which there is hypoplasia of the thymus, retention of normal parathyroid function, and possible varying degrees of humoral immunodeficiency. Bruton congenital agammaglobulinemia (choice A) is an Xlinked recessive disorder characterized by the failure of B-cell precursors to differentiate into mature B-lymphocytes, which are absent in the peripheral blood, lymph nodes, tonsils, and spleen. Serum immunoglobulin levels are decreased; however, the thymus and Tlymphocyte development are normal and cell-mediated immunity is intact. Chronic granulomatous disease of childhood (choice B) refers to a group of X-linked or autosomal recessive disorders characterized by different enzyme deficiencies of neutrophils and macrophages that lead to inhibition of hydrogen peroxide formation. Although still capable of bacterial phagocytosis, neutrophils and macrophages cannot kill bacteria, particularly

the catalase-positive species such as Staphylococcus, Serratia, and Salmonella, which destroy their own endogenous hydrogen peroxide by virtue of catalase production. The disease occurs chiefly in males who present with recurrent bacterial infections of the skin, lymph nodes, lungs, and bones; widespread abscesses and granulomas are present. Severe combined immunodeficiency disease (choice C) is one of the most dramatic forms of congenital immunodeficiency in which a defect of lymphoid stem cells leads to failure of development of both Band T-lymphocytes. Although probably an embodiment of several different inherited diseases, most patients with severe combined immunodeficiency have the autosomal recessive form, and greater than half of these lack the enzyme adenosine deaminase, resulting in the accumulation of lymphotoxic metabolites. Failure of both cellular and humoral immunity causes a variety of severe viral, bacterial, fungal, and protozoal infections early in life, with death usually occurring within the first year. Wiskott-Aldrich syndrome (choice E) is an X-linked recessive disease characterized by thrombocytopenia, eczema, and immunodeficiency; both cellular and humoral immunity is impaired. Progressive T-cell deficiency occurs despite a morphologically normal thymus, and serum IgM levels are low, although IgG levels are usually normal. Recurrent bacterial, viral, and fungal infections occur, particularly with S. pneumonia and Haemophilus influenzae as these organisms have polysaccharide antigens that mainly elicit IgM antibody response. Thrombocytopenia may be severe and approximately one-third of patients die from hemorrhage. Patients are prone to developing lymphoma.

QUESTION 464
A 28-year-old man has a long history of intermittent bloody diarrhea. The colon is surgically removed and displayed in below figure. The most likely diagnosis is which of the following?



A. amebic colitis
B. collagenous colitis
C. gangrenous colitis
D. pseudomembranous colitis
E. ulcerative colitis

Correct Answer: E

Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
The colon segment in figure demonstrates ulcerative colitis. The disease is limited to the colon and preferentially involves in continuity the rectum, sigmoid, and descending colon. The affected colon demonstrates a red, granular mucosa with occasional pseudopolyp formation. Deep fissures, skip lesions with alternating areas of diseased and normal colon, and strictures do not typically occur. Amebic colitis (choice A) is usually limited to the right colon and displays multiple, scattered, separate ulcerations. In collagenous colitis (choice B), the colon appears grossly normal. Gangrenous colitis (choice C) has an acute clinical course. Grossly, the colon demonstrates a transmural area of blackened, thinned tissue. Pseudomembranous colitis (choice D) is usually an acute colitis occurring after antibiotic therapy. White, custard-like debris that partially coats the mucosal surface is the characteristic gross observation of pseudomembranous colitis.

QUESTION 465
Five weeks after returning from visiting relatives in New England, a 22-year-old man develops severe headaches, fever, chills, fatigue, and multiples skin lesions. During the physical examination, the skin lesions are noted to be slightly raised and erythematous but are nontender. He states that a similar single lesion appeared on his thigh just before his return, but he was otherwise asymptomatic. Based upon this information, the most likely causative agent is which of the following?

A. Borrelia burgdorferi
B. Francisella tularensis
C. Rickettsia rickettsii
D. Toxoplasma gondii
E. Yersinia pestis

Correct Answer: A
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Lyme disease (caused by the spirochete B. burgdorferi) occurs worldwide but in the United States is found principally in northeastern and some mid-western states. It is transmitted by the Ixodes tick and the site of its bite is usually indicated by an expanding erythematous lesion with central clearing (erythema chronicum migrans (stage 1), which corresponds to the lesion the patient found just prior to his return home. Days or weeks following this stage, the organisms spread hematogenously and may cause secondary skin lesions, fever, chills, fatigue, severe headaches, arthralgias, and cardiac arrhythmias as well as many other findings (stage 2). It was at this point that the patient presented to is physician. Without treatment, many months later patients may enter stage 3 and develop more severe complications, including frank arthritis and encephalopathy. Tularemia is a zoonosis caused by F. tularensis (choice B); transmission occurs from contact with wild animals or biting insects. It is common in the southern Midwestern region. Infection typically results in an ulcerative lesion at the inoculation site and regional lymphadenopathy. R. rickettsii (choice C) causes Rocky Mountain spotted fever, the most severe of the rickettsial diseases. Intracellular infection of systemic and pulmonary endothelial cells via tick or insect vector causes a macular rash, appearing first on the wrists and ankles with subsequent spread to the full extremity and the trunk. Typically by 1 week lesions become hemorrhagic and form petechiae. Extensive microcirculatory infection may cause significant multisystemic effects, causing mortality in 35% of cases. Infection with the parasite T. gondii (choice D) is most often associated with immunocompromised patients; transmission typically occurs from ingestion of soil contaminated with cysts shed in cat feces or from undercooked meat. Common manifestations include

cervical lymphadenopathy in immunocompetent individuals and CNS involvement in the immunocompromised. Y. pestis (choice E) is the bacterium responsible for causing plague, a zoonotic disease carried by rats and wild rodents; it is transmitted to humans by bites from infected fleas. There are three forms of plague--bubonic, septicemic, and pneumonic. Bubonic is the most common, and is associated with a characteristic lymphadenopathy of rapid onset in which enlarging lymph nodes (buboes) become progressively painful and tender, often surrounded by considerable edema.

QUESTION 466
Alaboratory test for a newly discovered infectious disease is found to have a sensitivity of 90% and a specificity of 90%. The disease has a prevalence of 1%. The test is run on one of your patients and yields a negative result. What is the probability (to the nearest whole number) of this result being a true negative rather than a false-negative result (what is the predictive value negative)?

A. 1%
B. 10%
C. 50%
D. 90%
E. 100%

Correct Answer: E
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
In a population of 100,000, 1000 people will have the disease and 99,000 will be disease free (the prevalence of the disease equals 1%). The sensitivity equals 90%, which indicates that in a population of people with the disease, 90% will have a positive test result (true positives) and 10% will have a negative test result (false negatives). The specificity also equals 90%, which indicates that in a population of people without the disease, 90% will have a negative test result (true negatives) and 10% will have a positive test result (false positives). Thus, looking at the negative test results, there were 100 false negatives (10% of the 1000 people with the disease) and 89,100 true negatives (90% of the 99,000 people without the disease). Therefore the chances of the test result being a true negative = (true negatives)/(true negatives + false negatives) = (89,100)/(89,100 + 100) = 99.9% (= 100% to the nearest whole number). Mathematically, 1% (choice A), 10% (choice B), 50% (choice C), and 90% (choice D) can be eliminated.

QUESTION 467
A 34-year-old woman who has been taking oral contraceptives for many years presents with acute abdominal pain and fullness. Paracentesis harvests 200 mL of bloody fluid. Imaging studies show a 6- cm mass in the liver that is subsequently resected. Histological examination of this specimen would most likely reveal this to be which of the following?

A. angiosarcoma
B. cholangiosarcoma
C. focal nodular hyperplasia
D. hepatocellular carcinoma

E. liver cell adenoma

Correct Answer: E
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Liver cell adenomas may occur after several years of taking oral contraceptives but the actual mechanism of tumor formation is unknown. The clinical presentation is often acute abdominal pain due to necrosis of the tumor and hemorrhage. Given the patient's history, liver cell adenoma is by far the most likely choice. Angiosarcomas of the liver (choice A) are very rare tumors associated with exposure to vinyl chloride (used in the manufacture of the plastic polyvinyl chloride). Cholangiosarcomas (choice B) are rare tumors that arise in the intrahepatic bile ducts. However, they are more common in the Far East, where there is an association with the liver fluke, Clonorchis sinensis. Focal nodular hyperplasia (choice C) is a tumor-like lesion that occurs more frequently in women. It has a weak association with oral contraceptive use. On cut section, it typically has a central stellate scar. It is usually asymptomatic and is only resected in the symptomatic patient. Hepatocellular carcinoma (choice D) in the United States usually arises in a background of cirrhosis due either to alcoholism or HBV infection. However, worldwide, hepatitis B is the major etiologic factor and up to 50% of patients with hepatocellular carcinoma may be noncirrhotic.

QUESTION 468
A 71-year-old man presents to his primary care physician for a check-up accompanied by his wife, who reports that she had to "push him out of the door" to go to see a doctor as his last physical examination was almost 8 years ago. He states that he has been feeling well other than having some lower back pain. Physical examination reveals a firm, nodular prostate. On further questioning, the patient states that he has not noticed any change in urination. Laboratory studies reveal a mildly elevated serum prostate-specific antigen level and a serum alkaline phosphatase level almost three times normal. These findings are most consistent with which of the following?

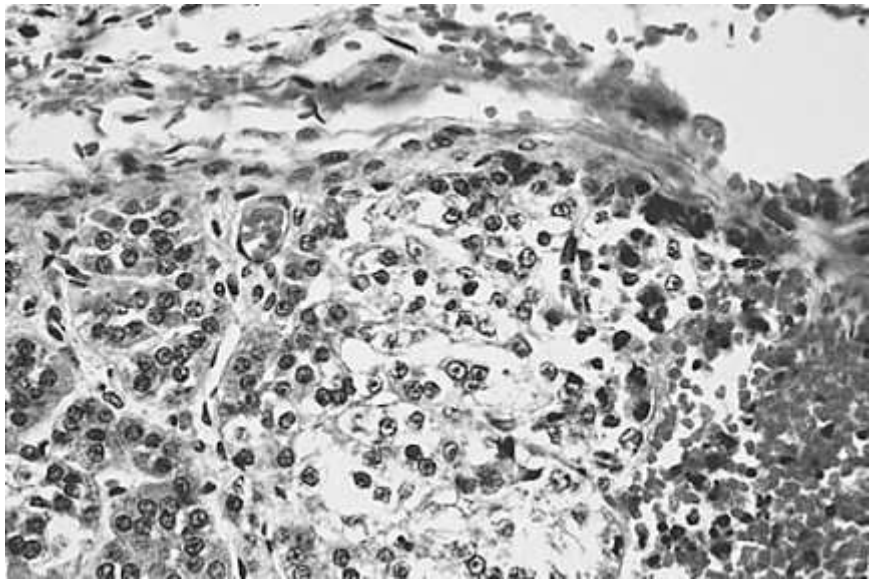
A. acute prostatitis
B. benign prostatic hyperplasia
C. chronic prostatitis
D. local invasion of the prostate by bladder carcinoma
E. metastatic prostate carcinoma

Correct Answer: E
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Serum prostate-specific antigen can be elevated in both benign prostatic hyperplasia and prostatic carcinoma (it is worth noting that both can also be within the reference range). However, this patient has a firm, nodular prostate with no urinary changes making carcinoma the more likely of the two. The additional finding of high levels of alkaline phosphatase is compatible with osteoblastic metastases. These findings taken together make metastatic prostate carcinoma the most likely of the choices given. Prostate-specific antigen can be elevated in acute prostatitis (choice A), benign prostatic hyperplasia (choice B), and chronic prostatitis

(choice C), but none of these conditions, or local invasion of bladder carcinoma (choice D) would be expected to produce the increase in alkaline phosphatase that is seen in this case.

QUESTION 469
A 3-day-old girl develops numerous skin lesions followed soon thereafter by severe encephalitis. Despite extensive treatment, she dies a few days later. An autopsy examination reveals that the infant has a systemic infection involving all major organs. The photomicrograph in below figure is taken from a section of adrenal gland. Which of the following is the most likely infectious agent?



A. cytomegalovirus
B. herpes
C. rubella
D. syphilis
E. Toxoplasma

Correct Answer: B
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:

Figure shows areas of necrosis and cell nuclei containing Cowdry A inclusions, indicating that this is a disseminated herpes infection acquired during passage through the birth canal. Cytomegalovirus (choice A), rubella (choice C), syphilis (choice D), and Toxoplasma (choice E) are the other members of the TORCHS complex, but are typically acquired transplacentally. Cytomegalovirus (choice A) has Cowdry A nuclear inclusions but, in addition, has multiple cytoplasmic inclusions and greatly increased cell size. The other agents do not generate Cowdry A inclusions.

QUESTION 470
On a routine, employment-related chest x-ray, a 26-year-old woman is found to have a solitary rib lesion appearing as a well-demarcated, radiolucent area with a ground glass appearance and cortical thinning. When questioned, the patient states that she has never experienced any pain and does not recall ever sustaining trauma to the area. Which of the following is the most likely diagnosis?

A. chondrosarcoma
B. Ewing sarcoma
C. fibrous dysplasia
D. osteogenesis imperfect
E. osteomalacia

Correct Answer: C
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
This woman's findings are consistent with a diagnosis of monostotic fibrous dysplasia (FD), variably considered to be either a benign tumor or a developmental disorder in which an abnormal proliferation of mesenchymal cells replaces normal cancellous bone with immature woven bone and fibrous tissue. In 70% of cases, a single bone is affected (monostotic FD), most frequently involving the ribs, long bones, or jawbones. Patients tend to be asymptomatic and are typically diagnosed between 2030 years of age by incidental radiograph findings (as described). Multiple bone involvement occurs in 30% of cases (polyostotic FD), often affecting shoulder and pelvic girdles and craniofacial bones. These patients tend to be younger (<10) and have a more severe course, often with pain, recurrent pathological fractures, and permanent skeletal deformity. Chondrosarcoma (choice A) has a peak incidence in the fourth to sixth decades and typically involves the flat bones of the pelvic and shoulder girdles. The histological classification of these tumors is complex. The majority of the tumors (~75%) fall into the "conventional" hyaline/ myxoid category; however, some of the minority classifications such as "mesenchymal" and "clear cell" may occur in much younger individuals. Most patients with Ewing sarcoma (choice B) are 1020 years of age. Although the femur and pelvic flat bones are common sites, similar to fibrous dysplasia, these tumors present as painful enlarging masses, which frequently are warm, swollen, and tender on examination. The x-ray appearance is also quite different, demonstrating an irregular destructive lesion extending into the surrounding soft tissues and a periosteal reaction layered in an "onion-peel" fashion. Osteogenesis imperfecta (choice D) results from a deficiency in the synthesis of type I collagen. The result is a patient with very brittle bones who manifests numerous fractures during childhood. Osteomalacia (choice E) arises from a deficiency of vitamin D (comparable to rickets in children), causing inadequate mineralization and excessive production of bone matrix (osteoid) that results in deformities of weightbearing bones. There are no focal lesions as seen in this patient.

QUESTION 471
Molecular studies on a certain carcinoma demonstrate DNA containing multiple sites of adjacent pyrimidine cross-linking to form pyrimidine dimers. This malignancy most likely arose in which of the following sites?

A. bladder
B. colon
C. lung
D. pancreas
E. skin

Correct Answer: E
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
DNApyrimidine dimer formation is a possible carcinogenic consequence induced by the ultraviolet (UV) component of solar radiation. UV radiation comprises three wavelength ranges that are designated UVA, UVB, and UVC. UVB is the principal fraction responsible for the induction of squamous cell carcinoma, basal cell carcinoma, and possibly malignant melanoma of the skin (UVC is also carcinogenic, but is more effectively absorbed by the ozone layer). Aberrant pyrimidine linkages are normally corrected by DNA repair genes (nucleotide excision pathway); however, some errors remain uncorrected if these mechanisms are overwhelmed by excessive sun exposure, potentially leading to transcription errors and oncogenesis. Bladder, colon, lung, and pancreatic cancers (choices AD) frequently arise from mutations in various RAS oncogene proteins, resulting in defective guanine triphosphate (GTP) enzyme activity and increased growth factor signal transduction.

QUESTION 472
A 66-year-old woman initially develops some subtle changes in memory, judgment, and behavior. However, this is followed by a very severe and rapidly progressive dementia that is accompanied by startle myoclonus. She dies 8 months after the original onset of her symptoms. Her disease is most likely the result of which of the following?

A. acquired or inherited prion
B. hereditary lysosomal storage disease
C. increased neurofibrillary tangles (NFTs)
D. protozoan infection
E. repeated exposure to a chemical toxin

Correct Answer: A
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Creutzfeldt-Jakob disease is caused by a prion that may either be inherited or acquired during life. Prions are composed of protein only and behave like a slow viral

infection. Human prion disease has recently become more prominent with the outbreak of mad cow disease in England due to human consumption of beef tainted with prions. Creutzfeldt- Jakob disease is not known to be inherited as a lysosomal storage disease (choice B) or to be caused by protozoan infections (choice D). Increased NFTs (choice C) are seen with Alzheimer's disease (AD), not Creutzfeldt- Jakob disease. Repeated exposure to chemical toxins (choice E) can cause dementia. Alcohol is a common example. However, the histology of chemical dementia usually differs in character and distribution from the cortical spongiform changes seen in Creutzfeldt-Jakob disease.

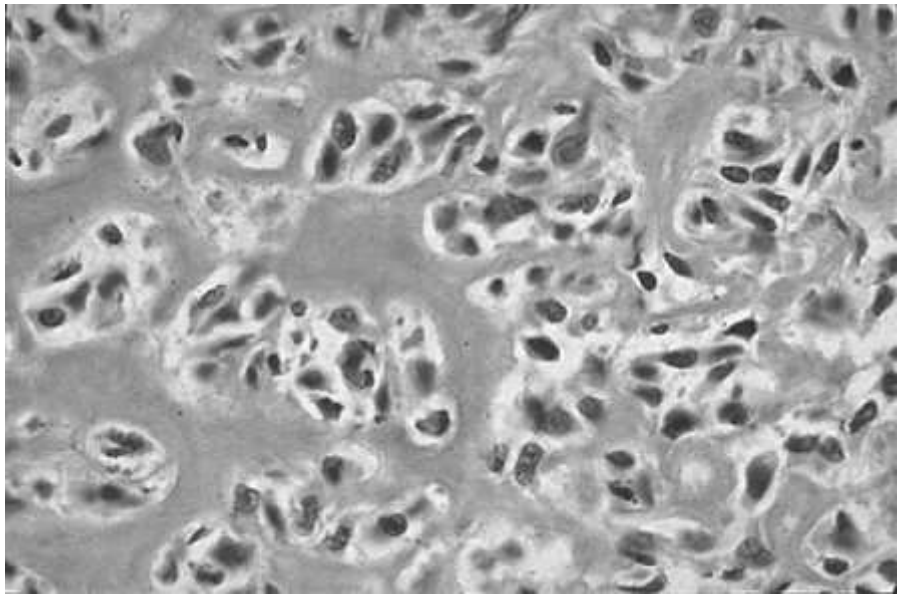
QUESTION 473
A 59-year-old man complains of periorbital edema and ankle swelling which has been gradually increasing over the past few months. Blood pressure is 120/80 mm Hg. Urinalysis shows a 4+ proteinuria but no cells or casts. Serum albumin is moderately decreased but blood urea nitrogen (BUN) and creatinine are normal. Which of the following is the most likely diagnosis?

A. acute proliferative glomerulonephritis
B. diabetic nephropathy
C. IgA nephropathy
D. lupus nephritis
E. membranous glomerulopathy

Correct Answer: E
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
This patient has nephrotic syndrome as indicated by the edema, 4+ proteinuria, and hypoproteinemia and the most common cause of this syndrome in adults is membranous nephropathy. Acute proliferative glomerulonephritis (choice A) produces a nephritic syndrome marked by a mild proteinuria, hematuria, azotemia, and hypertension. Diabetic nephropathy (choice B) does produce proteinuria that is sometimes sufficient to cause nephrotic syndrome, but hypertension is often present along with some indication of chronic renal failure neither of which are seen in this case. IgA nephropathy or Berger disease (choice C) is a cause of nephrotic syndrome but with hematuria often associated with an upper respiratory infection unlike the presentation in this case. Patients with lupus nephritis (choice D) may present with either nephritic or nephritic syndrome, but certainly this is a much less common cause of nephrotic syndrome than membranous glomerulonephritis.

QUESTION 474
A 16-year-old boy fractured his leg while running track at school. X-ray studies revealed an abnormality at the lesion site indicating that this was a pathological fracture. Abiopsy of the area was taken and a photomicrograph of the tissue is shown in below figure. The most likely diagnosis is which of the following?



A. chondroblastoma
B. chondrosarcoma
C. osteoid osteoma
D. osteoblastoma
E. osteochondroma
F. osteosarcoma

Correct Answer: F
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
This section in figure shows many large, hyperchromatic, pleomorphic cells that are producing osteoid, typical of an osteosarcoma. A chondroblastoma (choice A) would display sheets of primitive chondroblasts within a cartilage matrix that is irregularly calcified. Chondrosarcoma (choice B) most typically occur in the age range of 4060 with the most common locations being the pelvic girdle, ribs, shoulder girdle, and to a lesser extent the long bones, vertebrae, and sternum. Microscopically, the lower grade tumors will show chondroid differentiation whereas a grade 3 tumor may appear as a spindle cell tumor with little chondroid differentiation. Osteoid osteoma (choice C) and osteoblastoma (choice D) have a very similar microscopic appearance consisting of a random pattern of woven bone with many osteoblasts in evidence within a stroma of granulation-like tissue. Osteoid osteomas are small, very painful tumors that are found in teenagers and

young adults and respond very well to aspirin. It usually occurs in the long bones of the leg. Osteoblastomas are larger tumors that more usually affect the vertebrae. Osteochondromas (choice E) (or exostoses) are mushroom-like growths that usually bud from the metaphysic of long bones but may occur, less frequently, at many other sites. Microscopically, one sees irregular trabecular bone covered by a cartilaginous cap.

QUESTION 475
A 78-year-old woman is found to have a first morning urine specific gravity of 1.010. Assuming that she has not had anything to drink since yesterday evening, this is most indicative of which of the following?

A. acute pyelonephritis
B. advanced renal failure
C. diabetic glomerulosclerosis
D. hyperlipidemia
E. normal kidney function

Correct Answer: B
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Aurine specific gravity of 1.010 is the same as the specific gravity of glomerular filtrate (i.e., isosthenuric). Thus, this woman was not concentrating her urine overnight (usual SG > 1.020) which is an indication of severe renal damage as seen in advanced renal failure. Patients with acute pyelonephritis (choice A), diabetic glomerulosclerosis (choice C), and hyperlipidemia (choice D) who are not in advanced renal failure would still be expected to show some overnight concentrating ability as, of course, would normal kidney function (choice E).

QUESTION 476
A 26-year-old man is found dead in his apartment. A neighbor, who had seen him the previous day, said that he appeared to be perfectly healthy at that time. The coroner performs an autopsy and the only significant finding is hyperinflation of the lungs with areas of atelectasis and thick mucus in the bronchioles. Microscopically, there is thickening of the bronchial epithelial basement membranes, hyperplasia of submucosal mucous glands and bronchial smooth muscle, and infiltration by eosinophils. All of these findings are consistent with which of the following diagnoses?

A. adult respiratory distress syndrome
B. bronchiolitis obliterans--organizing pneumonia
C. chronic bronchitis
D. emphysema
E. status asthmaticus

Correct Answer: E
Section: Pathology and Path physiology

Explanation

Explanation/Reference:
Explanation:
Characteristic microscopic findings in asthma are thickened basement membranes, hyperplasia of bronchial smooth muscle, hyperplasia of submucosal mucous glands, and the presence of eosinophils, all of which were seen in this case. The hyperinflation of the lungs and mucous plugging are common gross findings in someone dying in status asthmaticus. The principal microscopic finding in adult respiratory distress syndrome (choice A) is the formation of hyaline membranes rather than the changes described above. Idiopathic bronchiolitis obliterans with organizing pneumonia (BOOP) (choice B) is often a difficult clinical diagnosis to make and may require a lung biopsy which will show connective tissue forming in alveoli and distal bronchioles. Chronic bronchitis (choice C) shows hyperplasia of the bronchial mucous glands and fibrosis of bronchial walls. Emphysema (choice D) is marked by the loss of alveolar walls, leaving large irregular air spaces.

QUESTION 477
A 74-year-old woman with left heart failure develops pulmonary edema. This accumulation of fluid is best explained by which of the following mechanisms?

A. decreased hydrostatic pressure
B. decreased lymphatic drainage
C. decreased oncotic pressure
D. increased hydrostatic pressure
E. increased lymphatic drainage
F. increased oncotic pressure

Correct Answer: D
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
In left-sided heart failure, poor chamber contractility results in impaired systolic outflow, creating an increase in end diastolic volume and a corresponding increase in ventricular hydrostatic pressure. Impaired ventricular emptying causes stasis in the pulmonary circulation, resulting in a similar increase in volume and pressure in the microvasculature. Capillary congestion leads to widening of endothelial intercellular junctions, leakage of fluid into the interstitium/ alveoli, and the formation of pulmonary edema. Decreased hydrostatic (choice A) and oncotic (choice C) pressures and increased lymphatic drainage (choice E) theoretically would reduce total blood volume, thus acting to retard, not induce, pulmonary edema. Decreased lymphatic drainage (choice B) and increased oncotic pressure (choice F) could potentially lead to pulmonary edema; however, they would be secondary factors in cases of left heart failure, as increased hydrostatic pressure is directly responsible for the accumulation of fluid in the lungs.

QUESTION 478
A 19-year-old freshman football player collapses during preseason workouts on a very hot afternoon. He has no significant prior medical history other than a recent upper respiratory infection. He is taken to the emergency room but cannot be revived. An autopsy reveals an enlarged heart that, on microscopic examination, shows myocyte disarray. Which of the following was the most likely cause of death?

A. alcoholism
B. cardiac amyloidosis
C. heat stroke
D. hypertrophic cardiomyopathy
E. viral myocarditis

Correct Answer: D
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Hypertrophic cardiomyopathy often presents with dyspnea and chest pain. Arrhythmias are a common problem in these individuals and sudden death, particularly after very strenuous exercise, can occur. There is good evidence that at least half of these cases are familial--probably autosomal dominant. Adistinctive microscopic finding is myocyte disarray. Alcoholism (choice A) can produce dilated cardiomyopathy which does not show myocyte disarray. Cardiac amyloidosis (choice B) would not be expected in a young adult with no history of chronic disease and would show interstitial hyaline deposits of amyloid microscopically. Heat stroke (choice C) is marked by a lifethreatening increase in core temperature and would not produce the changes described above. Viral myocarditis (choice E) can produce an enlarged flabby heart but does not have myocyte disarray

QUESTION 479
The changes seen in the kidney shown in below figure were an incidental finding in the autopsy of a 39-year-old woman. The most likely cause is which of the following?

A. abuse of analgesics
B. hypertension
C. postrenal obstruction
D. renal cell carcinoma
E. renal infarct

Correct Answer: C
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:

The kidney in figure demonstrates severe hydronephrosis characterized by dilation of the renal pelvis at the expense of the subadjacent renal medulla and cortex. Postrenal obstruction, such as a ureteral stone, is the most likely etiology. Abuse of analgesics (choice A) may be associated with necrosis of the renal papillae. The papillae in the photo are not necrotic. Hypertension (choice B) mainly affects the blood vessels of the renal cortex, sparing the pelvic region of the kidney. Renal cell carcinoma (choice D) displays a yellowish cortical-based tumor, not hydronephrosis. An acute renal infarct (choice E) demonstrates a pale, wedge-shaped area with its base along the renal capsule. A chronic infarct shows either fibrous scarring or cyst formation. The renal pelvis is usually unaffected by renal infarcts.

QUESTION 480
A 64-year-old man with long-standing hypertension experiences severe abdominal pain and loses consciousness. He dies en route to the hospital. Significant autopsy findings include dilation of the aorta just above the iliac bifurcation and massive abdominal hemorrhage. Which of the following was most likely the initiating event that resulted in his fatal lesion?

A. antibody-mediated endothelial damage
B. autosomal dominant inheritance of an abnormal gene on chromosome 15
C. intimal proliferation with fibrous cap formation
D. luminal narrowing of the vasa vasorum leading to medial degeneration and fibrosis
E. ossification of calcific deposits in the tunica media

Correct Answer: C
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
This man had a ruptured abdominal aortic aneurysm. Most commonly, this is the result of severe atherosclerotic changes that lead to weakening, dilation, and possible rupture of the affected aorta. (In this case, the hypertension would have accelerated the atherosclerotic changes and increased the likelihood of rupture of the aneurysm.) Initial vascular changes found in atherosclerosis include intimal thickening and fibrous cap formation. Antibodymediated endothelial damage (choice A) is a common cause of vasculitis but is not involved in atherosclerosis. Of the diseases that result from autosomal dominant inheritance of an abnormal gene on chromosome 15 (choice B), the most common is probably adult polycystic disease but this has no bearing on the development of atherosclerosis. Luminal narrowing of the vasa vasorum leading to medial degeneration and fibrosis (choice D) is seen in the development of a syphilitic aortic aneurysm but has no role in this patient's disease process. Ossification of calcific deposits in the tunica media (choice E) and other areas of dystrophic calcification may occur as a complication of atherosclerotic plaques, but even if present in this patient, this process would not represent the initiating event.

QUESTION 481
A 5-year-old boy is brought to a pediatrician by his mother for progressive abdominal girth and poor appetite. His mother is concerned over a "growing lump" she has felt in his abdomen, and physical examination confirms the presence of a large palpable mass in the left upper quadrant. Abdominal ultrasound demonstrates an 18-cm solid mass in the upper pole of the left kidney. Arenal biopsy is taken. Which of the following is the pathologist most likely to see on microscopic examination of the biopsy?

A. a mixture of proliferating smooth muscle cells, mature fat cells, and abnormalblood vessels

B. numerous fusiform cysts lined by uniform cuboidal cells and no normal parenchyma
C. primitive mesenchymal tissue with minimal tubular and glomerular differentiation
D. sheets of large cells with abundant clear cytoplasm and small uniform nuclei
E. well-formed papillary frond structures lined by cytologically normal, thickened epithelium

Correct Answer: C
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
A large tumor appearing in the pole of a kidney in a child of this age is almost certainly a Wilms' tumor. The microscopic appearance of this neoplasm can be highly variable with some areas resembling renal blastema, as well as epithelial and stromal areas. One usually sees attempts to form glomeruli and tubules. Amixture of proliferating smooth muscle cells, mature fat cells, and abnormal blood vessels (choice A) describes an angiomyolipoma. Numerous fusiform cysts lined by uniform cuboidal cells and no normal parenchyma (choice B) is the microscopic appearance of infantile polycystic disease. Sheets of large cells with abundant clear cytoplasm and small uniform nuclei (choice D) describe a renal oncocytoma. Well-formed papillary frond structures lined by cytologically normal, thickened epithelium (choice E) is a description that is compatible with a renal papillary adenoma.

QUESTION 482
Over the past few months, a 5-year-old boy has developed changes suggestive of puberty. Physical examination reveals the presence of secondary sex characteristics including pubic hair and penile enlargement. Laboratory studies reveal increased levels of ACTH. If you were able to examine his adrenals, which of the following would you most likely find?

A. bilateral atrophy of the cortex
B. bilateral atrophy of the medulla
C. bilateral cortical hyperplasia
D. bilateral medullary hyperplasia
E. nodule in the cortex
F. nodule in the medulla

Correct Answer: C
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
This child has one of a group of unusual diseases (congenital adrenal hyperplasia) in which there is an inherited deficiency of an enzyme in the biosynthetic pathway for the corticosteroids; most of these cases are due to a partial deficiency of 21-hydroxylase. The decreased feedback inhibition to the pituitary results in increased production of ACTH, resulting in bilateral adrenal cortical hyperplasia. Impairment of corticosteroid synthesis shunts more substrate into the sex steroid

pathway, leading to increased production of androgens (resulting in precocious puberty or virilism in a female child). Bilateral atrophy of the cortex (choice A) has a number of causes. Primary causes are unusual and tend to affect both glucocorticoid and mineralocorticoid production; however, secondary causes (e.g., exogenous steroids) are more common and tend to affect only glucocorticoid production. Precocious puberty is not seen. Bilateral atrophy of the medulla (choice B) with a normal cortex would be extremely unusual and would not be expected to produce precocious puberty. Bilateral medullary hyperplasia (choice D) has been reported but is very unusual and would also not produce precocious puberty. Anodule in the cortex (choice E) could be either a hyperplastic nodule or an adenoma. The former is asymptomatic and the latter is most unlikely to produce precocious puberty but, if it did, would probably also demonstrate hypercortisolism, which is not seen in this patient. A nodule in the medulla (choice F) could be a small, early pheochromocytoma but this would not produce precocious puberty.

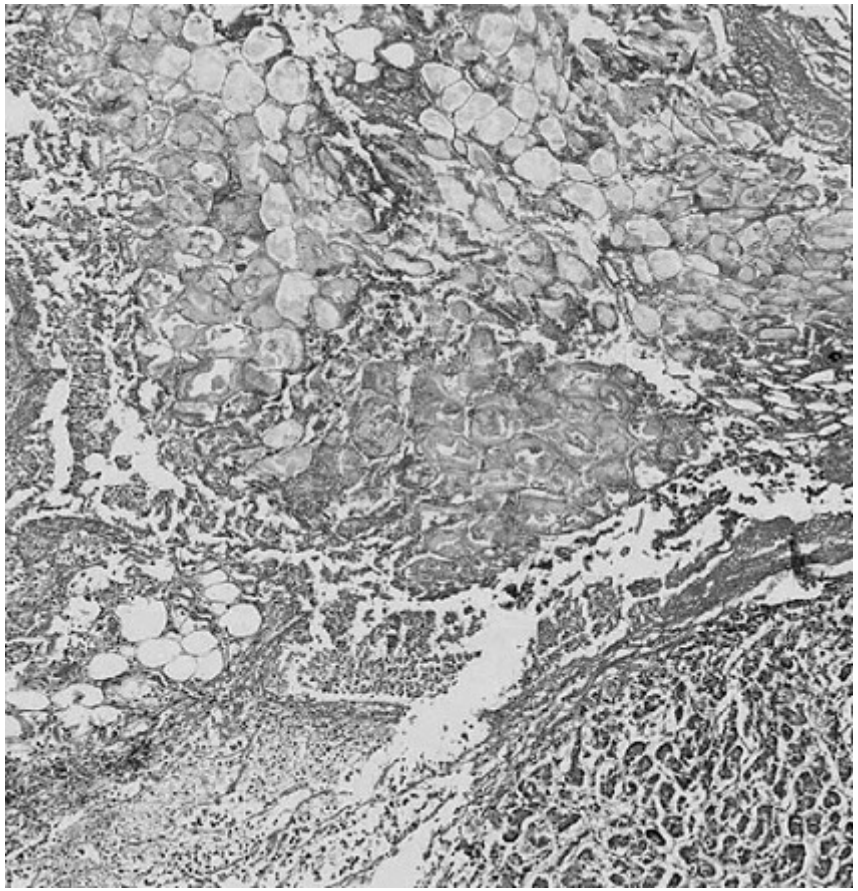
QUESTION 483
A 7-year-old girl presents with a neck mass located at the anterolateral aspect of the neck, anterior to the sternocleidomastoid muscle. A biopsy of the lesion revealed a largely cystic mass lined by stratified squamous epithelium surrounded by an underlying dense layer of lymphoid tissue with germinal centers. Based on these findings, what is the most likely diagnosis?

A. branchial cleft cyst
B. granulomatous lymphadenitis
C. Hodgkin lymphoma
D. metastatic laryngeal carcinoma
E. thyroglossal duct cyst

Correct Answer: A
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
A cystic structure in the lateral neck lined by squamous or, less usually, columnar epithelium and surrounded by lymphoid issue with germinal centers is invariably a branchial cleft cyst. Granulomatous lymphadenitis (choice B) should demonstrate granulomatous inflammation in a lymph node which is not described here. Hodgkin lymphoma (choice C) occurs in five subtypes, none of which is associated with epithelial tissue. Metastatic laryngeal carcinoma (choice D) is usually squamous cell in origin and would demonstrate pleomorphic polygonal cells with "prickles" and "pearls." A thyroglossal duct cyst (choice E) can have a histological appearance very similar to that of a branchial cleft cyst but the most important difference is the midline location of the thyroglossal duct cyst.

QUESTION 484
A 45-year-old man developed severe abdominal pain and was transported to the emergency room where he was found to be hypotensive and in shock. He was unresponsive to therapy and died 2 days later. Based upon this history and the accompanying image in below figure, which of the following most likely initiated this sequence of events?



A. acute pancreatitis
B. esophageal varices
C. gastric ulcer
D. liver cirrhosis
E. splenic infarct

Correct Answer: A
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
In the lower left corner of figure is pancreas while the rest is composed of necrotic fat cells, some viable fat cells, and inflammatory exudate. Thus, the initiating event in this case is acute pancreatitis. The image does not show any of the other organs listed, thereby ruling out choices B through E.

QUESTION 485
Approximately 6 months ago, a 59-year-old man developed a dull, continuous abdominal pain that radiated to the right upper quadrant and was relieved by bending forward. He has also had recurrent thrombophlebitis. He now develops jaundice. Of the following, which is the condition that would most likely explain all of these findings?

A. alcoholic cirrhosis
B. cholecystitis
C. cholelithiasis
D. pancreatic adenocarcinoma
E. viral hepatitis

Correct Answer: D
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Carcinomas in the head of the pancreas often obstruct the ampulla of Vater and the common bile duct, producing jaundice; carcinoma in the body and tail do not obstruct and remain clinically silent much longer. A dull, continuous abdominal pain is also a typical symptom and many patients report that the pain decreases when they lean forward. About 10% of patients with pancreatic carcinoma develop a migratory thrombophlebitis known as Trousseau syndrome. Alcoholic cirrhosis (choice A), cholecystitis (choice B), cholelithiasis (choice C), and viral hepatitis (choice E) may all be associated with abdominal pain and jaundice, but not the other findings in this case.

QUESTION 486
A 67-year-old man complains of low back pain and generalized weakness, gradually worsening over the past 6 months. Physical examination reveals an individual in moderate discomfort due to the back pain. Laboratory examination reveals an anemia with rouleaux formation of the erythrocytes on the peripheral smear. Urinalysis demonstrates proteinuria and hypercalciuria. X-rays reveal diffuse osteoporosis of the spine and small lytic lesions in the ribs. Which of the following diagnoses most likely explains these findings?

A. fibrous dysplasia
B. iron-deficiency anemia
C. metastatic prostatic carcinoma
D. multiple myeloma
E. osteosarcoma

Correct Answer: D
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
This is a patient with multiple myeloma and one of the earliest symptoms of the disease is back pain. These patients have increased levels of Ig in the blood (which produces an increased erythrocyte sedimentation rate and will be seen as rouleaux formation on the blood smear) and light chains (Bence Jones protein) in the urine. Multiple myeloma causes multifocal osteolytic lesions throughout the skeletal system and these are apparent on x-rays and are also responsible for the hypercalcemia as the ongoing bone destruction releases calcium. Fibrous dysplasia (choice A) is a disorder of bone in children with progressive replacement of a localized area of bone by an abnormal proliferation of benign fibrous tissue and bony trabeculae composed of haphazardly arranged woven bone. It occurs as a monostotic and polyostotic form, but neither could account for the findings in this case. Iron- deficiency anemia (choice B) does not produce any of the findings in this case. Metastatic prostatic carcinoma (choice C) can spread quite easily to the lumbar-sacral spine and this causes back pain. However, these bone lesions are osteoblastic rather than osteolytic. Osteosarcoma (choice E) is typically found in teenagers or young adults. When seen in older individuals, it usually occurs in association with Paget disease of the bone.

QUESTION 487
A 67-year-old woman complains of gradually increasing fatigue. On physical examination, she is found to be anemic and has a peripheral neuropathy characterized by loss of position and vibratory sense. Laboratory studies document a macrocytic anemia and decreased WBC and platelets counts. What pathological mechanism accounts for these findings?

A. a diet deficient in folate
B. autoantibodies against parietal cells or intrinsic factor
C. chronic blood loss
D. diabetes mellitus
E. myelodysplastic sideroblastic anemia

Correct Answer: B
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
The clinical and laboratory findings suggest a diagnosis of pernicious anemia. Almost all cases are due to autoantibodies against parietal cells or intrinsic factor. These autoantibodies disrupt the normal absorption of vitamin B12. The inability to absorb vitamin B12 leads to a macrocytic pancytopenia and peripheral neuropathy. A diet deficient in folate (choice A) can cause a macrocytic anemia, but there are no concomitant neurological findings. Chronic blood loss (choice C) usually results in microcytic hypochromic anemia due to iron deficiency. Anemia and peripheral neuropathy commonly occur with diabetes mellitus (choice D). However, the anemia is normocytic and the neuropathy is sensory. Myelodysplastic sideroblastic anemia (choice E) may present hematologically with a macrocytic pancytopenia. A peripheral neuropathy is not seen.

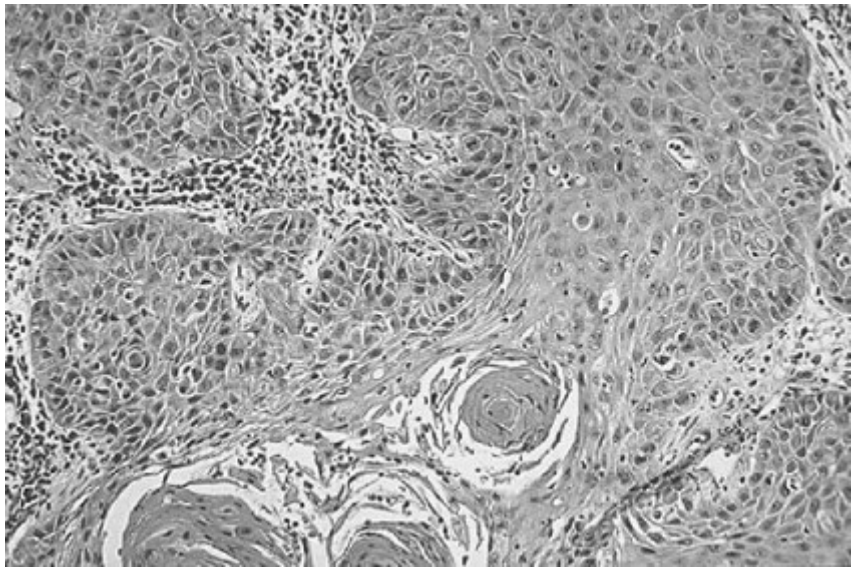
QUESTION 488
A 27-year-old woman complains of double vision and drooping of her eyelids. She also states that she has recently noticed weakening of her jaws when chewing tough foods. Physical examination reveals mild weakness of her facial and neck muscles but no atrophy is noted. Which of the following diagnoses is most likely?

A. conjunctivitis
B. myasthenia gravis
C. orbital inflammatory pseudotumor
D. Parkinson's disease
E. polymyositis

Correct Answer: B
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Myasthenia gravis is an autoimmune disease characterized by autoantibodies to acetylcholine receptors, and weakness of both facial and ocular muscles. Conjunctivitis (choice A) defines an inflammatory or infectious condition of the conjunctiva, and is not consistent with this clinical scenario. Orbital inflammatory pseudotumor (choice C) is a benign mass lesion of the eye region and is not associated with muscle weakness and autoantibodies. Parkinson's disease (choice D) is a neurologic movement disorder that does not demonstrate either weakness or acetylcholine autoantibodies. Polymyositis (choice E) is a subacute inflammatory disease of skeletal muscle, typically affecting proximal muscle groups, and specifically does not include facial muscles.

QUESTION 489
During a routine dental examination of a 55-year-old man, a small, reddish, and raised lesion is noted on the posterior of the median sulcus of his tongue. The patient is referred to a surgeon who performs an excisional biopsy of the lesion. A section of the biopsy is shown in below figure. Which of the following is the most appropriate diagnosis?



A. amyloidosis
B. candidiasis
C. inverted papilloma
D. leukoplakia
E. squamous cell carcinoma

Correct Answer: E
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
In figure, the pleomorphism of the nuclei and the clearly invasive nature of these cells indicate the malignant nature of this lesion. Furthermore, three keratin "pearls" at the bottom of the image and the sheets of cells, many with discernable intercellular bridges (prickles), allow one to recognize this as a squamous cell carcinoma. Amyloidosis (choice A) can affect many organs including the tongue. However, amyloid would appear as acellular, eosinophilic deposits around vessels and in the parenchyma of tissues which is not seen here. Candidiasis (choice B) is commonly seen on the tongue, but is not invasive in a person with an intact immune system. Its appearance is that of pseudohyphae with yeast forms. Inverted papilloma (choice C) is a benign but locally aggressive tumor found in the nose and paranasal sinuses but not seen in the tongue. Leukoplakia (choice D) of the oral cavity appears as a white patch that cannot be scraped off and cannot be otherwise identified. This is not the gross description given for this patient.

QUESTION 490

A 47-year-old gardener receives an insect sting while pruning some rose bushes. Within a few minutes the area around the sting is swollen and red. The swelling is mostly the result of which of the following?

A. decreased plasma oncotic pressure
B. increased hydrostatic pressure
C. increased vascular permeability
D. lymphatic obstruction
E. venous obstruction

Correct Answer: C
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Following tissue injury (in this case caused by the insect sting), vasoactive inflammatory mediators originating from both cellular and humoral sources are released at the site of injury. These produce vasodilation of arterioles and increased blood flow producing the redness, and increased vascular permeability of enules allowing the formation of an exudates that produces swelling. All of the other choices can produce edema, but do not feature an increase in vascular permeability (they produce noninflammatory edema). Decreased plasma oncotic pressure (choice A) can result from either excessive loss (e.g., nephrotic syndrome) or decreased synthesis (e.g., cirrhosis, protein malnutrition) of plasma proteins, principally albumin. Increased hydrostatic pressure (choice B) occurs, for example, in heart failure where the pressure builds up behind the failing pump. Lymphatic obstruction (choice D) occurs where there is blockage to the normal lymphatic drainage. This could be due to the growth of an obstructing cancer or to inflammation and fibrosis (e.g., postsurgery, filariasis). Venous obstruction (choice E) leads to increased hydrostatic pressure as the blood backs up behind the obstruction.

QUESTION 491
The prevalence for disease X is 1%. Anew laboratory test is positive in 99% of the patients with disease X, but half of the total of positive test results obtained correspond to patients without disease X. Based on this information, the test would be classified as which of the following?

A. sensitive and nonspecific
B. sensitive and specific
C. nonsensitive and nonspecific
D. nonsensitive and specific

Correct Answer: B
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:

Let us take a population of 100,000 individuals. Since the prevalence of disease X is 1%, 1000 individuals have disease X and 99,000 are disease-free. The test is positive in 99% of individuals with the disease (i.e., of the 1000 with disease, there are 990 true positives and 10 false negatives), thus the test is clearly sensitive. However, half of all positive test results are occurring in disease-free individuals. If 990 individuals with disease had a positive test result (true positives), then there must also be 990 disease-free individuals who had a positive test result. It was stated above that 99,000 are disease-free, so of these 990 have a positive test result (false positives) and the remainder (99,000 990 = 98,010) must have a negative test result (true negatives). Specificity may be defined as the percentage of individuals in a disease-free population who have a negative test result. This is mathematically equivalent to (true negatives)/(true negatives + false positives) = (98,010)/(98,010 + 990) = 98,010/99,000 = 99%. Thus the test is both sensitive and specific, and the other answers (choices A, C, D, and E) are incorrect.

QUESTION 492
A 47-year-old woman has a 3-month history of fatigue and pruritus. A percutaneous liver biopsy reveals a nonsuppurative, granulomatous distention of medium-sized intrahepatic bile ducts. What is the most common etiology of this disorder?

A. acquired vascular abnormality
B. alcohol abuse
C. autoimmune disease
D. parasitic infection
E. viral infection

Correct Answer: C
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Primary biliary cirrhosis is an autoimmune disorder. Autoantibodies against mitochondria are usually present. Hyperbilirubinemia, steatorrhea, portal hypertension, and osteomalacia may be seen in the later stages of the disease. Vascular abnormalities (choice A), alcohol abuse (choice B), parasitic infections (choice D), and viral infections (choice E) all may mimic the clinical picture of primary biliary cirrhosis. They are not, however, the usual etiologic agents.

QUESTION 493
A 5-year-old girl has had numerous childhood fractures. She is also found to have blue sclera, hearing abnormalities, and misshapen teeth. Which of the following is the most likely cause of these findings?

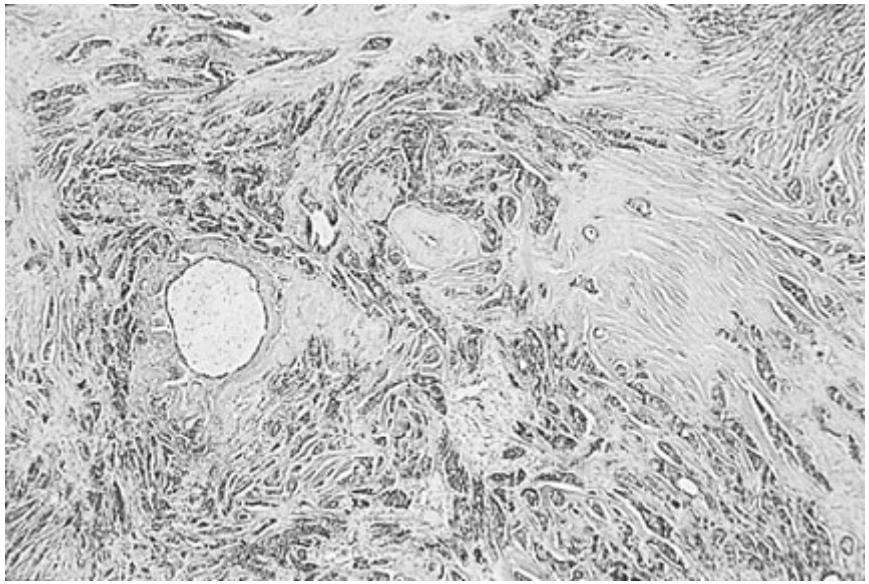
A. abnormal intestinal receptors for calcium
B. an inability to metabolize vitamin D
C. inadequate mineralization of bone matrix
D. renal inability to conserve phosphorous
E. synthesis of abnormal type I collagen

Correct Answer: E

Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Osteogenesis imperfecta type I, is a genetic disorder characterized by synthesis of an abnormal type I collagen. Frequent childhood fractures, blue sclera, poor hearing, and misshapen teeth may all occur clinically because of the abnormal collagen synthesis. Abnormal intestinal receptors for calcium (choice A), inability to metabolize vitamin D (choice B), inadequate mineralization of bone matrix (choice C), and renal inability to conserve phosphorous (choice D) are not the primary pathologic alterations responsible for this disorder.

QUESTION 494
A 53-year-old woman recently noticed a firm, 2-cm nodule in her right breast during monthly self- examination. The histology of her breast biopsy tissue is displayed in below figure. Which of the following is an adverse prognostic indicator that may be seen with this disorder?



A. estrogen receptor positive
B. low S phase
C. overexpression of Her2/neu oncogene
D. progesterone receptor positive
E. well-differentiated histology, grade I of III

Correct Answer: C
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Overexpression of NEU oncogene in invasive breast carcinoma (shown in figure) is an adverse prognostic indicator. Breast cancers that are estrogen-receptor positive (choice A), have a low S phase (choice B), are progesterone-receptor positive (choice D), and are well differentiated (choice E), considered to have more favorable prognostic implications. Size of the primary breast carcinoma and the status of the axillary lymph nodes are also major factors that influence the prognosis of invasive ductal breast adenocarcinoma.

QUESTION 495
A 17-year-old boy presented to his orthopedist complaining of progressive knee pain for 3 months. Physical examination revealed a swollen, warm, and tender right knee. Serum alkaline phosphatase levels were increased. Right knee x-ray revealed a lytic lesion in the metaphyseal area of the knee extending into the proximal diaphysis, and elevation of the periosteum with new bone production. Microscopically, biopsy demonstrated haphazard osteoid formation, pleomorphic cells with hyperchromatic nuclei, and tumor giant cells. Based on this information, what is the most likely diagnosis?

A. chondrosarcoma
B. Ewing sarcoma
C. giant cell tumor
D. malignant fibrous histiocytoma
E. osteosarcoma

Correct Answer: E
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
In a 17-year-old boy, the anatomical location and the x-ray findings are very typical of osteosarcoma. In this case, the tumor has broken through the cortex, elevated the periosteum with reactive periosteal bone formation (the characteristic triangular shadow seen on x-ray is known radiographically as Codman triangle). The microscopic findings of pleomorphic cells with hyperchromatic nuclei, tumor giant cells, and bone formation confirm the diagnosis. Chondrosarcomas (choice A) most typically occur in the age range of 4060 with the most common locations being the pelvic girdle, ribs, shoulder girdle, and to a lesser extent the long bones, vertebrae, and sternum. Microscopically, the lower grade tumors will show chondroid differentiation, whereas a grade 3 tumor may appear as a spindle cell tumor with little chondroid differentiation. Ewing sarcomas (choice B) occur in children and young adults and usually originate in long bones, ribs, pelvis, and vertebrae. Microscopically one sees small, uniform, oval to round cells with hyperchromatic nuclei and little cytoplasm, which may appear clear due to glycogen abundance. Giant cell tumors (choice C) usually occur in the age range of 2040 most commonly originating in distal femur, proximal tibia, distal radius, and proximal humerus, but virtually any bone may be affected. These are usually benign tumors that can, however, be locally aggressive; roughly 410% do metastasize and these must be considered as malignant. Not surprisingly, the microscopic appearance is marked by the presence of many giant cells that have an osteoclast-like, syncytial appearance. Malignant fibrous histiocytomas (choice D) are fibroblastic, collagen-producing bone tumors that may also arise from soft tissues; indeed, they are the most common type of soft tissue sarcoma. They occur more frequently in the middle-aged and elderly but have been reported at all ages. Microscopically, lesions

reveal spindle cells arranged in a whorled pattern with variable amounts of collagen deposition; also present may be large, plump cells (resembling histiocytes), tumor giant cells, many mitoses, and a chronic inflammatory infiltrate.

QUESTION 496
A 71-year-old man was diagnosed with prostate cancer approximately 1 year ago. At that time he weighed 182 lbs (with a height of 75 in). He has progressively lost weight since then and is now found to weigh 148 lbs. Although he reports a moderate loss of appetite, it does not correlate with his total weight loss. Which of the following mediators is most likely contributing to this patient's decrease in weight?

A. C-reactive protein
B. vomplement 3a protein
C. interleukin-2
D. parathyroid hormone-related protein
E. tumor necrosis factor

Correct Answer: E
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Progressive weight loss, anorexia, and weakness comprise the wasting syndrome known as cachexia that is often associated with cancer. Although patients report anorexia and abnormalities in taste, the reduction in caloric intake does not sufficiently explain the often profound degree of wasting. While the mechanism is poorly understood, cancer frequently causes an increased metabolic rate that is postulated to occur as a result of cytokine production by both the tumor and the host response to the umor. Avariety of cytokines may function synergistically to cause cachexia; however, experimental animal studies suggest that tumor necrosis factor is the major contributor. C-reactive protein and complement 3a protein (choices Aand B) both act as opsonins in acute inflammation, while interleukin-2 (choice D) is an important growth factor for the proliferation of T-lymphocytes. Parathyroid hormonerelated protein (choice E) production is responsible for causing the hypercalcemia paraneoplastic syndrome associated with certain malignancies, most notably carcinomas of the lung and kidney.

QUESTION 497
A 21-year-old previously healthy man had a headache, malaise, and low-grade fever for the past 4 days. He was brought to the emergency room this morning after he started behaving in an unusual manner and experienced difficulty in speaking. While he was being transported, he suffered a generalized seizure. Physical examination showed a fever of 103℉ and total disor ientation. Deep tendon reflexes were exaggerated and the plantar response was bilaterally extensor. He had mild neck stiffness and the optic fundi showed early papilledema. Alumbar puncture produced clear CSF under an opening pressure of 300 mm O. Protein was 160 mg/dL, glucose 66 mg/dL (blood glucose 90

H_2

mg/dL), and there were 32 mononuclear cells/L. No PMNs were present. Which of the following is the most likely cause of this man's condition?

A. glioblastoma multiforme

B. herpetic meningoencephalitis
C. meningioma
D. meningococcal meningitis
E. spontaneous cerebral hemorrhage
F. subarachnoid hemorrhage

Correct Answer: B
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
The presence of neck stiffness, the increase in the amount of protein, and the number of cells in the CSF confirm the presence of meningitis. However, the unusual behavior, disorientation, seizure, speech disorder, and abnormal reflexes represent involvement of various parts of the cerebral cortex. Thus this is an acute inflammation of the meninges and brain or a meningoencephalitis. This also accounts for the very high CSF pressure since there is brain edema in addition to the meningitis. The somewhat more prolonged course and the presence of mononuclear cells in the CSF are evidence for viral etiology making herpes the best choice of those listed and eliminating meningococcal meningitis (choice D) which elicits PMNs in the CSF and does not produce encephalitis. Tumors (choices Aand C) and hemorrhage (choices E and F) would not give this clinical presentation or CSF results.

QUESTION 498
A 46-year-old obese woman has had symptoms of vulvovaginitis for the past 9 months that is found to be caused by Candida. Laboratory tests reveal proteinuria and glucosuria, and increased serum glucose, BUN and creatinine. If a renal biopsy were performed, which of the following would be the most likely light and electron microscopic findings, respectively, in the glomeruli?

A. hypercellularity with thickened basement membranes (GBM); duplication of GBM
B. hypercellularity with PMNs; subepithelial deposits
C. normocellularity with thickened GBM; subepithelial deposits
D. normal morphology; loss of epithelial foot processes
E. thickened GBM; no deposits

Correct Answer: E
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
An obese woman presenting with chronic candidal vulvovaginitis should certainly be suspected of having diabetes, and the laboratory results confirm this diagnosis. A renal biopsy of this patient would be expected to show glomerular basement membrane thickening and focal and diffuse glomerulosclerosis by light microscopy, but electron microscopy would not show any electron-dense deposits since antigen-antibody complexes are not formed in diabetes. Hypercellular glomeruli with

thickened and duplicated basement membranes (tram tracks; train tracks) (choice A) is found in membranoproliferative glomerulonephritis type 1. Hypercellular glomeruli with PMNs and subepithelial deposits (humps) (choice B) are an indication for postinfectious (poststreptococcal) glomerulonephritis. Normocellular glomeruli with thickened basement membranes and subepithelial deposits (spikes) (choice C) are found in membranous glomerulopathy. Normal morphology by light microscopy with loss of epithelial foot processes by electron microscopy is a classic finding of nil disease.

QUESTION 499
An overweight, 46-year-old man has complained of heartburn for the past 2 years. A biopsy of his lower esophagus is displayed in below figure. Which of the following is the most likely diagnosis?

A. Barrett esophagitis
B. Candida esophagitis
C. granulomatous esophagitis
D. PlummerVinson syndrome
E. viral esophagitis

Correct Answer: A
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:

Barrett esophagitis is a metaplastic alteration of the lower esophagus in response to chronic acid reflux. Figure displays the specialized type of Barrett esophagitis, complete with numerous goblet mucous cells. Candida esophagitis (choice B) does not contain glandular epithelium. Squamous epithelium, yeast, and pseudohyphae are expected instead. Granulomatous esophagitis (choice C) and viral esophagitis (choice E) are not characterized by metaplastic glandular epithelium. Giant cells or inclusion bodies may be seen, depending on the etiology. Plummer-Vinson syndrome (choice D) describes the formation of a lumenal web in the upper third of the esophagus. Microanatomy displays squamous epithelium, not metaplastic glandular epithelium.

QUESTION 500
A 47-year-old man has had a cough that produces yellowish sputum for the past week. He is found to have a total WBC count of 16,300 per L with a differential count of 75% segmented neutrophils, 11% band neutrophils, 9% lymphocytes, 4% monocytes, and 1% eosinophils. His temperature is 100℉ and chest x-ray reveals a lesion in the right lower lobe that has a central cavity and an air-fluid level. Which of the following is the most likely diagnosis?

A. bronchogenic carcinoma
B. interstitial pneumonia
C. lobar pneumonia
D. pulmonary abscess
E. pulmonary tuberculosis

Correct Answer: D
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
The productive cough and leukocytosis with a high percentage of neutrophils and bands indicates that this is a bacterial infection and, of the choices given, is most likely an abscess. Bronchogenic carcinoma (choice A) can obstruct an airway and produce infection, but there is no evidence presented to support this. Interstitial pneumonia (choice B) is typically caused by Mycoplasma or viruses and produces a mononuclear response rather than a neutrophilic response; the cough is usually nonproductive. Lobar pneumonia (choice C) fills the affected lobe with exudate, but does not typically result in necrosis or abscess formation. Pulmonary tuberculosis (choice E) can produce a cavitary lesion, typically at the apices, but also is marked by a mononuclear response.

QUESTION 501
A 23-year-old woman develops a sore throat, chills, headache, coryza, and a nonproductive cough. A chest x-ray reveals an indistinct, patchy interstitial infiltrate. She has an uneventful recovery within a few days without receiving therapy. Which of the following outcomes is most likely to occur in the region of the affected lung?

A. healing by first intention
B. metaplasia
C. repair by scar formation
D. resolution
E. subacute inflammation

Correct Answer: D
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Resolution, or restoration of tissue to its preinjury state, occurs in tissue injury where minimal cell necrosis has occurred, such as this case of interstitial pneumonia. Removal of debris associated with the accompanying acute inflammatory response is sufficient to restore parenchymal tissue to its normal state. Regeneration of new parenchymal cells will occur to replace necrotic cells provided the involved cells have: (i) regenerative capacity; (ii) exist in remaining sufficient viable number, and (iii) possess an adequate connective tissuesupporting framework. Healing by first intention (choice A), also known as primary union, describes healing of skin wounds in which the edges are in close apposition, such as a surgical incision. Metaplasia (choice B), the replacement of one mature cell type by another mature cell type abnormal to that location, occurs most commonly in epithelial tissues where chronic physical or chemical irritation is present, such as squamous metaplasia of the endocervix or bronchial mucosa, and intestinal metaplasia of the esophagus. Repair by scar formation (choice C) occurs either in injured tissue comprised of permanent cells (e.g., myocardium), when resolution fails to occur in acute inflammation, or if chronic inflammation persists with ongoing necrosis. Subacute inflammation (choice E) describes repeated attacks of acute inflammation in which incomplete resolution of individual attacks leads to increasing chronic inflammation with superimposed acute inflammation.

QUESTION 502
An 89-year-old man develops a persistent cough with increasing dyspnea. He worked in the shipyards during his 20s, is a lifelong smoker, and has a positive purified protein derivative (PPD) skin test. During the physical examination, a pleural effusion is detected and subsequently drained. Laboratory analysis reveals a specific gravity of 1.013, protein of 1.4 g/dL, and a small number of macrophages. Based upon these laboratory values, which of the following is the most likely diagnosis for this patient?

A. heart failure, left-sided
B. heart failure, right-sided
C. lung infection, bacterial
D. lung infection, tuberculous
E. primary malignancy, squamous cell
F. primary malignancy, mesothelioma

Correct Answer: A
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Pleural effusion that has a specific gravity less than 1.012 and a protein concentration of less than 1.5 g/dL is classified as a transudate and is associated with circulatory problems (increased hydrostatic pressure, decreased oncotic pressure, lymphatic obstruction). Exudates usually have a specific gravity >1.020 and protein concentration higher than 3 g/dL and are associated with inflammatory or neoplastic processes. Based upon the laboratory results, the patient has a

transudate which rules out infection (choices C and D) and neoplasms (choices E and F). The persistent cough and dyspnea indicate that the fluid is accumulating in his lungs, which occurs in left-sided heart failure. Apure right- side heart failure would be expected to produce a systemic rather than pulmonary edema.

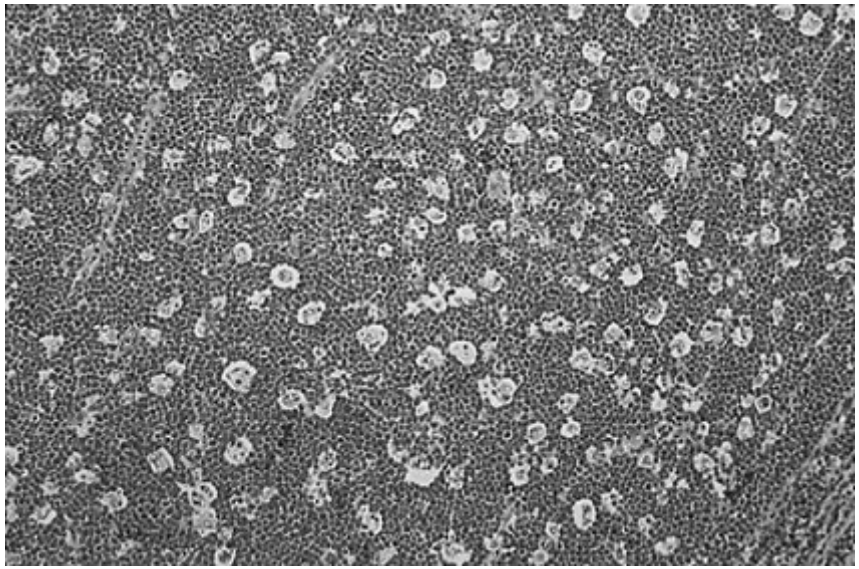
QUESTION 503
An 81-year-old man who contracted syphilis while serving in World War II is now found to have a saccular aneurysm of the thoracic aorta. The pathogenesis of this lesion is best explained by which of the following?

A. endarteritis obliterans of the vasa vasorum with subsequent mural ischemia
B. hypersensitivity reaction with multinucleated giant cells and mural fibrinoid necrosis
C. immune complex formation and complement activation
D. intimal fibroplasia and lipid deposition
E. medial cystic necrosis

Correct Answer: A
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Syphilitic saccular aneurysms of the thoracic aorta result from endarteritis obliterans of the vasa vasorum with subsequent mural ischemic necrosis. Hypersensitivity reactions, multinucleate giant cells, and fibrinoid necrosis (choice B) play no significant role in the development of syphilitic aortic aneurysms. Immune complex formation and complement activation (choice C) may be seen with tertiary syphilis, but involve only the small vessels, without aneurysm formation. Intimal fibroplasias and lipid deposition (choice D) are the early lesions of atherosclerosis. Cystic medial necrosis (choice E) is a noninfectious disorder characterized by abnormally weak connective tissue in the aortic media and deposits of myxoid substances.

QUESTION 504
A 12-year-old boy develops a large facial tumor. The histology of the lesion obtained from a fineneedle biopsy is displayed in below figure. The most likely diagnosis is which of the following?



A. adenocarcinoma
B. Burkitt lymphoma
C. chronic lymphocytic leukemialymphoma
D. parasitic lymphadenitis
E. salivary gland lymphoepithelioma

Correct Answer: B
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
The fine-needle biopsy shown in figure demonstrates a fairly monomorphic population of small, mitotically active neoplastic lymphocytes with associated starry sky histiocytes. The morphology of the tumor and the clinical history are typical for endemic Burkitt lymphoma. The diagnosis of adenocarcinoma (choice A) is incompatible with the photograph because malignant epithelial elements are not seen. Chronic lymphocytic leukemialymphoma (choice C) is distinctly uncommon in children and features mature lymphocytes without a starry sky background. There are no parasitic elements (choice D) evident in the photograph. Salivary gland lymphoepithelioma (choice E) is usually seen in an older age group, contains some remaining epithelial elements, and has larger immunoblastic-type lymphocytes.

QUESTION 505
A 76-year-old man with a long history of coronary artery disease presents to the emergency room with progressive substernal chest pain over the past 4 hours. He is short of breath and reports pain in his left jaw and shoulder area. His vital signs include blood pressure of 146/90 mm Hg, respiration rate of 20 per minute, pulse

of 98 per minute, and normal temperature. An initial ECG demonstrates ST elevation changes and a baseline troponin I level of 2.8 ng/mL. He is admitted to the coronary care unit for treatment. Four hours post-admission, the patient reports having no chest pain or dyspnea and is resting comfortably. His vital signs are stable. Which of the following complications are you most concerned about occurring in this patient within the next 24 hours?

A. cardiac tamponade
B. cardiogenic shock
C. holosystolic murmur
D. systemic thromboembolism
E. ventricular arrhythmia

Correct Answer: E
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
The findings in this patient confirm the diagnosis of an acute MI. While all of the given choices are potential post-MI complications, they differ in incidence and temporality. Ventricular arrhythmias are the most common complication, occurring in >75% of cases; they typically arise in the first 3 days following an MI, but are especially frequent in the first 24 hours. Cardiac tamponade (choice A) can develop with rupture of the left ventricular free wall and is frequently fatal; although this is most likely to occur within the first 48 hours, incidence is far lower compared to arrhythmias (~ <10%). Cardiogenic shock (choice B) may occur at any time, either as an early post-MI event (24 hours) with large infarctions or secondary to later complications (37 days); however, incidence is estimated at roughly 10%, and patients suffering from early cardiogenic shock would have signs of hypotension and pulmonary edema. Post-MI holosystolic murmurs (choice C) may develop secondary to mitral valve regurgitation (infrequently, tricuspid valve regurgitation) stemming from rupture of a papillary muscle, or from potential rupture of the interventricular septum; these are both rare events (12%). Systemic thromboembolism (choice D) is a potential consequence of mural thrombus formation, which develops as a result of endocardial injury and stasis caused by poor myocardial contractility; incidence of both events is fairly common (2040%). Mural thrombi typically form within the first 12 weeks post-MI; systemic thromboemboli may occur at any point after formation of a mural thrombosis, and do not adhere to any particular time course.

QUESTION 506
A 43-year-old man complains of a 25-lbs weight gain over the past 2 years distributed mostly in the trunk and face. He also states that he has developed abdominal stretch marks and facial acne during the same time period. Physical examination reveals BP 160/100 mm Hg and pulse 90 per minute. Significant laboratory tests were fasting glucose 145 mg/dL and 24-hour urinary free cortisol greatly increased at 390 g/d. The dexamethasone suppression test showed suppression of the urinary free cortisol at high but not low doses. Based upon this information, you would expect to find a hormonally- active tumor in which of the following sites?

A. adrenal cortex
B. adrenal medulla
C. anterior pituitary
D. posterior pituitary

Correct Answer: C

Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
This patient has the physical stigmata of excess cortisol or Cushing syndrome which is confirmed by the urinary free cortisol levels. Cortisol also has some mineralocorticoid activity producing sodium and water retention and hypertension. Cortisol promotes gluconeogenesis leading to glucose intolerance, hyperinsulinism and, in some patients, frank diabetes. The fact that urinary cortisol levels were suppressed by high but not low doses of dexamethasone strongly suggests a pituitary-based Cushing syndrome due to excess ACTH production or Cushing disease. ACTH-producing cells or corticotropes are found in the anterior pituitary. The dexamethasone suppression test rules out the adrenal (choices Aand B) as a site for the tumor and posterior pituitary (choice D) is not the location of the ACTH- producing cells.

QUESTION 507
A 38-year-old woman has experienced the gradual onset of a goiter. Serum T4 and T3 are within the reference range and thyroid-stimulating hormone (TSH) is slightly increased. Serum antithyroid peroxidase (antimicrosomal) antibodies are detected but there are no TSH receptor antibodies. Which of the following is the most likely diagnosis?

A. chronic autoimmune thyroiditis
B. Graves disease
C. primary atrophy of the thyroid
D. riedel struma
E. subacute thyroiditis

Correct Answer: A
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Patients with chronic autoimmune thyroiditis or Hashimoto disease may demonstrate several different serum thyroid autoantibodies, but these vary from patient to patient. Thyroid peroxidase antibodies are found in roughly 85% of patients with Hashimoto disease, about 40% of patients with Graves disease, and in <15% of patients with other thyroid disorders. The absence of TSH receptor antibodies rules out Graves disease (choice B), making Hashimoto disease the most likely diagnosis. Primary atrophy of the thyroid (choice C) and Riedel struma (choice D) are not usually associated with the formation of thyroid autoantibodies. Thyroid autoantibodies are only found transiently in a few patients with subacute thyroiditis (choice E) making this choice unlikely.

QUESTION 508
A 25-year-old woman discovers a breast lump during self-examination. On physical examination you identify a firm, round, movable, non-tender mass in the upper outer quadrant of the left breast. Your provisional diagnosis would be which of the following?

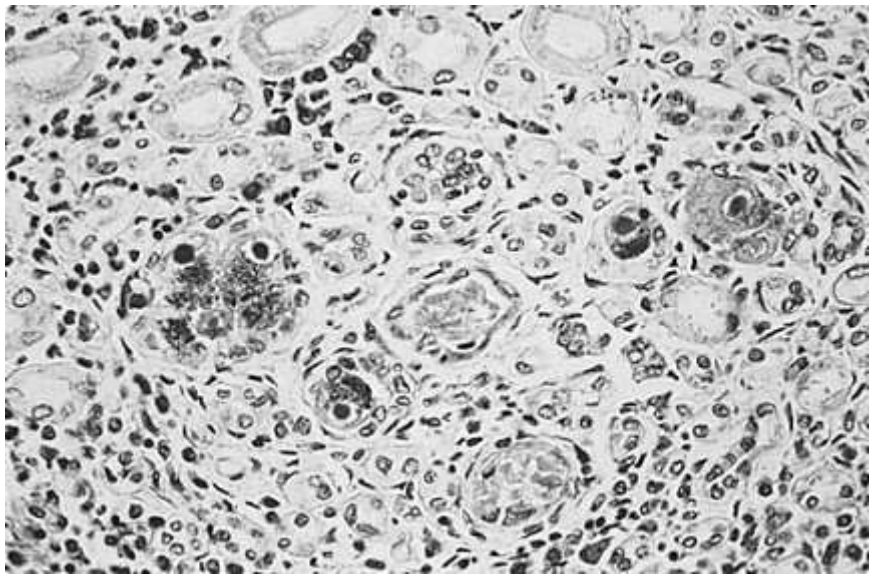
A. carcinoma

B. fibroadenoma
C. fibrocystic change
D. glandular hyperplasia
E. liposarcoma

Correct Answer: B
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
A single, firm, non-tender, freely movable breast mass in a woman of this age is most likely a fibroadenoma but, of course, this would need to be confirmed. These same factors make carcinoma (choice A) much less likely. Fibrocystic change (choice B) and glandular hyperplasia (choice D) would be expected to be bilateral rather than a single, isolated mass. Liposarcoma of the breast is very rare.

QUESTION 509
A 46-year-old woman with a 30-year history of juvenile diabetes undergoes a left renal allograft for advanced diabetic nephropathy. The transplant is initially successful; however, 3 months later she develops an unproductive cough with associated arthralgia, malaise, diarrhea, and fever of 101.6℉. Upon hospital admission, she is found to be leukopenic. The patient continues to decompensate and dies 3 days following admission. A section of her right kidney taken at autopsy is shown in below figure. This figure indicates an infection with which of the following agents?



A. cytomegalovirus
B. Epstein-Barr virus
C. Human immunodeficiency virus
D. Pneumocystis carinii
E. S. epidermidis
F. Streptococcus pyogenes

Correct Answer: A
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Opportunistic infections can occur in posttransplant patients on immunosuppressive therapy. figure shows greatly enlarged renal tubular cells containing both nuclear and multiple cytoplasmic inclusion bodies. These findings in combination are diagnostic of cytomegalovirus infection. Epstein-Barr virus (choice B) has been associated with a number of diseases, including infectious mononucleosis, Burkitt lymphoma, and nasopharyngeal carcinoma. However, even though this is also a herpes virus, it does not give the morphologic appearance described. Human immunodeficiency virus (choice C) does not produce inclusion bodies in infected cells. P. carinii (choice D) is an opportunistic fungus that can cause pneumonia in immunocompromised individuals, particularly AIDS patients. It may be visualized with silver staining methods. S. epidermidis (choice E) and S. Pyogenes (choice F) are bacteria that one would not associate with this histologic appearance.

QUESTION 510
A 3-day-old male infant is diagnosed with meconium ileus. You should be concerned that he has which of the following conditions?

A. alkaptonuria
B. cystic fibrosis
C. hemophilia A
D. phenylketonuria
E. Wilson disease

Correct Answer: B
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Meconium ileus is a very common early clinical expression of cystic fibrosis. Increased sweat sodium chloride level confirms the diagnosis. About 70% of children with cystic fibrosis have a deletional abnormality of chromosome 7. Pancreatic insufficiency, recurrent pulmonary infections, and biliary obstruction may complicate the disorder. Alkaptonuria (choice A) is an autosomal recessive disease that causes abnormal pigmentation and degeneration of cartilage. Hemophilia A(choice C)

is an X- linked hereditary disease caused by a relative lack of coagulation factors VIII or IX. Phenylketonuria (choice D) is due to a hereditary lack of the enzyme phenylalanine hydroxylase. Mental retardation is the major clinical finding. Wilson disease (choice E) is an autosomal recessive disorder of copper accumulation that principally affects the liver and brain.

QUESTION 511
A 29-year-old woman presents with weakness, fatigue, easy bruising, and nosebleeds. Analysis of her blood reveals a reciprocal translocation between chromosomes 22 and 9, and low leukocyte alkaline phosphatase levels. These findings confirm a diagnosis of which of the following?

A. acute lymphoblastic leukemia
B. Burkitt lymphoma
C. chronic myelogenous leukemia
D. follicular lymphoma
E. Hodgkin lymphoma

Correct Answer: C
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Ninety percent of individuals with chronic myelogenous leukemia have an acquired Philadelphia chromosome abnormality consisting of a translocation between chromosomes 22 and 9. The translocation places the proto-oncogene c-abl from chromosome 9 next to the breakpoint cluster region (bcr) on chromosome 22. The unique gene sequence bcr-abl confers a growth advantage with subsequent clonal expansion. Acute lymphoblastic leukemia (choice A) does not have a known reproducible gross chromosomal derangement. Burkitt lymphoma (choice B) is associated with a translocation of the c-myc oncogene from chromosome 8 to chromosome 14. Follicular lymphoma (choice D) is associated with a translocation between chromosomes 14 and 18. Hodgkin lymphoma (choice E) is characterized by the presence of ReedSternberg cells and has a number of subtypes.

QUESTION 512
A 35-year-old apparently healthy man undergoes a medical examination while applying for life insurance. He is not anemic. His hemoglobin electrophoresis is reported as: HbA, 62%; HbS, 35%; HbF, 1%; HbA2, 1%; no variant C, D, G, or H bands detected. The most likely diagnosis is which of the following?

A. sickle-cell disease
B. sickle thalassemia minor
C. sickle trait
D. thalassemia major
E. thalassemia minor

Correct Answer: C
Section: Pathology and Path physiology

Explanation

Explanation/Reference:
Explanation:
Individuals with sickle trait are healthy and not anemic. Hemoglobin electrophoresis demonstrates a minor proportion of hemoglobin S and a major proportion of hemoglobin A. Fetal hemoglobin and A2 hemoglobin are usually normal. Sickle trait confers the benefit of protecting erythrocytes from some forms of malarial infection. About 9% of blacks in the United States have sickle trait. In sickle cell disease (choice A), almost all hemoglobin is hemoglobin S. No hemoglobin A is detected and patients have a clinical history of severe anemia. Sickle thalassemia minor (choice B) presents as a chronic microcytic anemia with a major hemoglobin S component and elevated hemoglobin A2. Thalassemia major (choice D) and thalassemia minor (choice E) do not demonstrate hemoglobin S on electrophoresis.

QUESTION 513
A 37-year-old man visiting a third world country drinks from a fecally contaminated source of water. During the next week he has gradually increasing fever, anorexia, myalgia, and headache. He subsequently develops a maculopapular rash on his abdomen and his fever increases to 104℉ with abdominal pain and splenomegaly. During the third week, his condition rapidly deteriorates with intestinal bleeding, shock, and death. An autopsy reveals ulcerations overlying the Peyer patches of the small intestine, one of which is perforated. Which of the following is the most likely diagnosis?

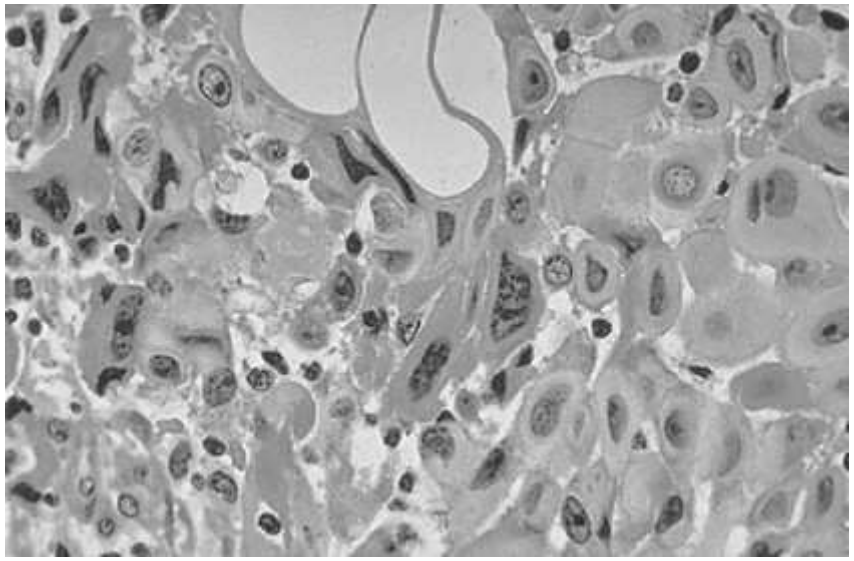
A. amebiasis
B. cholera
C. cryptosporidiosis
D. giardiasis
E. typhoid fever

Correct Answer: E
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
This is a case of typhoid fever. During the prodromal stage there is a gradual, step-like increase in fever with malaise, anorexia, myalgia, and headache. By the second week, the fever usually plateaus and the patient is very sick. There may be constipation or diarrhea with abdominal pain and distention, weakness, and a maculopapular rash (rose spots), particularly on the abdomen. If there are no complications, the patient may gradually improve over the next 2 weeks. One of the classic pathologic findings in typhoid is intestinal ulcerations over hyperplastic and necrotic Peyer patches. These may perforate and hemorrhage, as in this patient. Amebiasis (choice A) can produce a range of symptoms from being subclinical to producing fulminant dysentery. However, it involves the large bowel rather than the small intestine and produces flask-shaped ulcers separated by areas of normal bowel. Cholera (choice B) does not actually invade the intestinal epithelium and therefore causes insignificant microscopic changes and no ulceration. Cryptosporidiosis (choice C) causes a severe, chronic diarrhea in AIDS patients. The protozoa attach to the brush border of the intestinal epithelial cells but do not cause ulceration. Giardia (choice D) attaches to duodenal epithelial cells, but does not invade those cells and does not cause ulceration.

QUESTION 514
Aretroperitoneal mass was discovered during exploratory surgery on a 49-year-old woman. A photomicrograph of a section taken from the mass is shown in below

figure. Which of the following terms would be most appropriate to describe its appearance?



A. anaplasia
B. aplasia
C. dysplasia
D. hyperplasia
E. metaplasia

Correct Answer: A
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
The cells in figure show dramatic differences in the size, shape, and staining intensity of nuclei as well as differences in the cells overall, which allows one to say that they are pleomorphic. An additional factor is the lack of differentiation of these cells such that the cell type cannot be recognized, which is the definition of anaplasia. Aplasia (choice B) is a lack of growth of the anlage or primordium of an organ. Dysplasia (choice C) at the cellular level refers to disorderly maturation, usually of an epithelium. Hyperplasia (choice D) is an increase in the number of cells and this process may be either physiological or pathological. Metaplasia (choice E) is the replacement of one mature cell type by another (e.g., columnar epithelium being replaced by squamous epithelium in a smoker's lung).

QUESTION 515

Parents of an 18-month-old boy bring their child to their pediatrician as they are concerned about their son's recurring skin and lung infections. Biopsy of one of the boy's current skin lesions reveals the presence of neutrophils, lymphocytes, and scattered epithelioid cell granulomas. Culture of the lesion is positive for Staphylococcus aureus. Which of the following would best account for this patient's condition?

A. absence of T-helper cell activity
B. adenosine deaminase enzyme deficiency
C. complement C3b opsonization abnormality
D. decreased hydrogen peroxide production
E. defective macrophage phagocytosis

Correct Answer: D
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Decreased hydrogen peroxide production is associated with chronic granulomatous disease of childhood, a group of X-linked or autosomal recessive disorders associated with defects in genes that encode for different components of NADPH oxidase, the enzyme required for hydrogen peroxide production by neutrophils and macrophages. Impaired killing of intracellular organisms by neutrophils and macrophage leads to persistent cell-mediated immunity and granuloma formation as a second line of defense against organisms that are normally eradicated by an acute inflammatory response. As previously mentioned (see answer to question 624), patients are more susceptible to infections with catalase-positive species such as Staphylococcus, Serratia, and Salmonella, which destroy their own endogenous hydrogen peroxide by virtue of catalase production. Absence of T-helper cell activity (choice A), as occurs with human immunodeficiency virus infection, would not allow for the presence of epithelioid cell granulomas, as was shown on this biopsy, as this process is dependent on activated T-cell lymphokine production. Adenosine deaminase enzyme deficiency (choice B) is associated with severe combined immunodeficiency in which failure of both B and T lymphocytes occurs. Complement C3b opsonization abnormality (choice C) and defective macrophage phagocytosis (choice E) would result in abnormalities of immune phagocytosis, and here again would not be consistent with the histological finding of epithelioid cell granulomas, in which macrophages have phagocytosed the infectious bacteria.

QUESTION 516
A 57-year-old man has just returned from an overseas trip and reports having had severe substernal chest pain 3 days ago. Which of the following is the most appropriate laboratory test to order for this patient?

A. aspartate aminotransferase
B. creatine kinase, MB fraction
C. creatine kinase, total
D. lactate dehydrogenase, LD1 fraction
E. lactate dehydrogenase, total
F. troponin I

Correct Answer: F
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Troponin I is now the method of choice for the laboratory diagnosis of MI. There is a detectable increase within 48 hours of the infarction and the peak level is reached within 1436 hours. Levels do not return to baseline for 310 days making it an appropriate test for this patient who was 3 days post- infarction. Aspartate aminotransferase (choice A) was the first serum enzyme marker used for the diagnosis of MI, but it has poor specificity and sensitivity compared to newer markers and is no longer used for this purpose. Creatine kinase, total (choice C) is not used for the diagnosis of MI since the cardiac fraction (MB) can be overwhelmed by the presence of the skeletal muscle fraction. Creatine kinase-MB (choice B) is still being used in some institutions but it returns to baseline in 23 days and would not be useful for this patient. Lactate dehydrogenase, either LD1 fraction (choice D) or lactate dehydrogenase, total (choice E) return to baseline later than creatine kinase but have been replaced by troponin I and are seldom used.

QUESTION 517
A 48-year-old man with a long history of chronic viral hepatitis secondary to chronic hepatitis B virus (HBV) infection presented with a 2-month history of weight loss. Physical exam showed a cachectic man in mild distress. Scleral icterus and abdominal distension were present. Workup showed the presence of two mass lesions within the liver on ultrasound, which were confirmed on CT scan. Laboratory values revealed the following: AST 161 U/L; ALT U/L 188; total bilirubin 6.8 mg/dL; direct bilirubin 4.9 mg/dL; alkaline phosphatase 245 U/L; total protein 5.9 g/dL; albumin 2.8 g/dL; HBsAg positive; anti-HBs negative; anti- HCV negative; alpha-fetoprotein 7200 ng/mL. Aneedle biopsy of one of the mass lesions was performed under CT guidance. Which of the following is the most likely diagnosis?

A. fholangiocarcinoma
B. focal nodular hyperplasia
C. hepatocellular carcinoma
D. liver cell adenoma
E. metastatic carcinoma

Correct Answer: C
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
One of the potential consequences of chronic hepatitis B (and C) infection is the development of hepatocellular carcinoma, and the presence of the mass lesions with high levels of alphafetoprotein makes this extremely likely in this case and will be confirmed by the needle biopsy. Cholangiocarcinoma (choice A) is unusual in the United States but has a much higher incidence in Asia in association with infestation by the liver fluke, C. sinensis. Focal nodular hyperplasia (choice B) is a mass lesion of the liver, but is not a true neoplasm. It has a characteristic central scar and microscopically resembles cirrhosis. Liver cell adenoma (choice D) typically occurs in women taking oral contraceptives. Metastatic carcinoma (choice E) is certainly a possibility but given the clinical history of this case plus the high alpha-fetoprotein and the lack of any evidence for a primary malignant tumor elsewhere, hepatocellular carcinoma remains the most probable diagnosis.

QUESTION 518

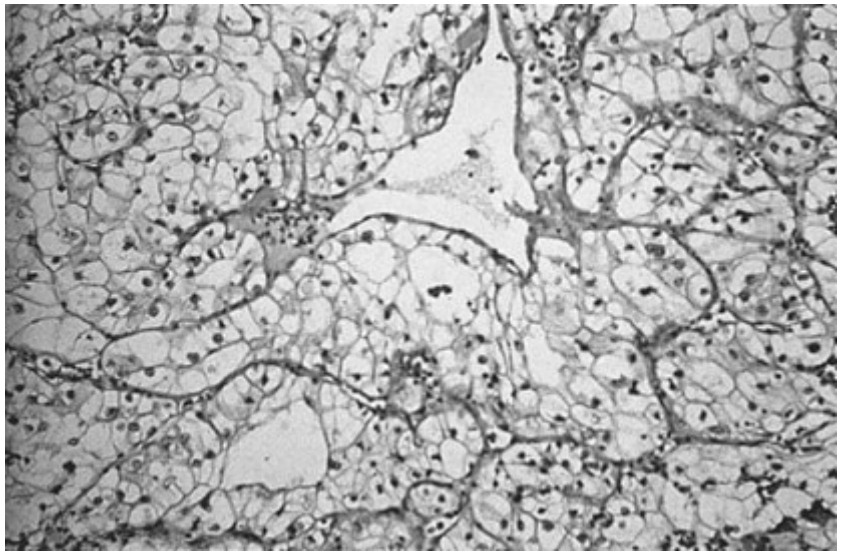
A 14-year-old, severely physically disabled individual is now on a respirator. His first 4 years of life were medically uneventful. Over the last 10 years, he has suffered from increasing symmetric muscle weakness that first affected the pelvic girdle and now involves almost all muscle groups. Several years ago, the calf portion of his legs appeared enlarged and on biopsy demonstrated fatty pseudohypertrophy with random alternating muscle fiber atrophy and hypertrophy. Which of the following is the most likely diagnosis?

A. cerebral palsy
B. muscular dystrophy
C. myositis ossificans
D. poliomyelitis
E. trichinosis

Correct Answer: B
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
The clinical scenario describes a classic example of Duchenne muscular dystrophy. The weakness is symmetric and most often begins at the pelvic girdle. Fatty pseudohypertrophy with alternating muscle fiber atrophy and hypertrophy typify the histologic changes. Many patients die before reaching their 20s. The other diagnostic options, cerebral palsy (choice A), myositis ossificans (choice C), poliomyelitis (choice D), and trichinosis (choice E), do not fit the clinical picture.

QUESTION 519
A 64-year-old man presents to his family physician with hematuria and flank pain. A radiology study identifies a renal mass. Aphotograph of this renal lesion's histology is displayed in below figure. The kidney mass is most likely which of the following?



A. angiomyolipoma
B. oncocytoma
C. renal cell carcinoma
D. transitional cell carcinoma
E. xanthogranulomatous pyelonephritis

Correct Answer: C
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Figure shows a clear cell adenocarcinoma, which is the most common histologic appearance for renal cell carcinoma. The patient's age, gender, and clinical presentation are typical for this malignant neoplasm. Angiomyolipoma (choice A) is a benign renal tumor that displays a mixture of blood vessels, smooth muscle, and mature fat on microscopic examination. Oncocytoma (choice B) is a benign renal neoplasm constructed by monomorphic cells with granular eosinophilic cytoplasm. Transitional cell carcinoma (choice D) usually arises in the renal pelvis and histologically is composed of anaplastic transitional cells without a clear cell adenocarcinoma component. Xanthogranulomatous pyelonephritis (choice E) is a benign inflammatory condition of the kidney that may produce a mass effect. The gross appearance, but not the microscopic appearance, may be confused with renal cell carcinoma.

QUESTION 520
A 79-year-old woman presents with a complaint of chronic and progressive mid-back pain for several months but no other symptoms. Spinal x-rays reveal two

compression fractures of the T10 vertebral body. Calcium, phosphate, and alkaline phosphatase levels are all within normal range. Histological examination of the affected vertebral bone would most likely reveal which of the following?

A. bony necrosis with acute and chronic inflammation and granulomas
B. disorganized interconnecting trabeculae of woven bone rimmed by osteoblasts
C. thickened, irregular trabeculae with prominent cement lines
D. thinning of the cortical and trabecular bone
E. widened osteoid seams of peripheral trabeculae

Correct Answer: E
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
This woman is suffering from senile, or postmenopausal, osteoporosis. In such patients, the calcium and phosphate levels will typically be within the reference range. The alkaline phosphatase will also usually be normal, but may be increased following fractures. Microscopic examination of affected bones will reveal loss of bone mass tending to affect horizontal more than vertical trabeculae. Bony necrosis with acute and chronic inflammation and granulomas (choice A) occurs in tuberculosis infection of the spine, where it is referred to as Pott disease. Disorganized interconnecting trabeculae of woven bone rimmed by osteoblasts (choice B) describes the appearance of an osteoblastoma, a benign bone tumor that is histologically very similar to and often described in conjunction with an osteoid osteoma. A characteristic difference between these two benign bone tumors is that osteoid osteomas are very painful lesions (excess prostaglandin E production) that respond dramatically to aspirin, while osteoblastomas produce a dull, achy pain that does not respond to aspirin. Thickened, irregular trabeculae with prominent cement lines (choice C) describe the morphology seen in Paget disease. Widened osteoid seams of peripheral trabeculae (choice E) reflect the appearance of unmineralized osteoid found in osteomalacia. Alkaline phosphatase levels are typically increased in osteomalacia (and rickets) and Paget disease.

QUESTION 521
A 52-year-old woman has experienced personality change and headaches over the past 3 months and is now developing a right hemiparesis. CT scan shows a mass in the left temporal lobe. Her condition deteriorates rapidly and she dies 7 months later. At autopsy, a large, hemorrhagic, necrotic tumor is identified in the left temporal lobe with extension to the right hemisphere. Microscopically there are highly pleomorphic cells with frequent mitoses. Serpentine areas of necrosis can be seen surrounded by masses of tumor cells. Which of the following is the most likely diagnosis?

A. ependymoma
B. glioblastoma multiforme
C. medulloblastoma
D. meningioma
E. oligodendroglioma

Correct Answer: B
Section: Pathology and Path physiology

Explanation

Explanation/Reference:
Explanation:
Glioblastoma multiforme is the most malignant astrocytoma and is also the most common intracranial primary neoplasm. It is typically a large tumor with areas of necrosis and hemorrhage and extends to the contralateral side of the brain (butterfly tumor). Microscopically the tumor is very pleomorphic with giant cells, palisading necrosis, and endothelial proliferation. The prognosis is universally poor. Ependymoma (choice A) is somewhat more common in children and originates from the ependymal cells lining the ventricles and central canal of the spinal cord. It is a slowgrowing tumor but has the ability to seed via the cerebrospinal fluid. Medulloblastoma (choice C) is principally a highly malignant tumor of childhood that originates in the cerebellum and has the well-known ability to metastasize via the cerebrospinal fluid. Meningioma (choice D) is a benign tumor arising from the arachnoid cap cells. However, it may involve the dura and calvaria making complete removal difficult. The tumor is only considered malignant if it grows into the underlying brain. Oligodendroglioma (choice E) occurs in adults and typically arises from the white matter of the cerebrum. Most of these tumors have areas of calcification which may be seen on x-ray. Many of these tumors are mixed tumors showing areas of astrocytoma.

QUESTION 522
A 73-year-old man is brought to his primary care physician by his wife who is concerned about her husband's progressive memory problems over the past year. She notes that he originally began forgetting to do his normal household chores, and then started routinely misplacing things around the house; he has also forgotten to close or lock doors or turn off the oven and has left the car running in the garage. He is having trouble remembering the driving routes to familiar places and names of longtime friends and acquaintances. The patient's neurological examination reveals disorientation to place and time, inability to recall three objects, and difficulty following a threestage command. Based on this information, which of the following best explains the pathogenesis of his condition?

A. cortical atrophy with neuronal cytoskeletal abnormalities and abnormal filamentous protein aggregation
B. gray matter damage to mammillary bodies and hemorrhage associated with nutritional deficiency
C. infiltrative mass of pleomorphic cells with areas of pseudopalisading, necrosis, and endothelial cell proliferation
D. injury of oligodendroglial cells with focal areas of demyelination, mononuclear infiltrate, and patchy gliosis
E. selective neuronal loss secondary to excitotoxicity associated with excessive glutamate levels

Correct Answer: A
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
This patient's symptoms are very consistent with a diagnosis of AD, the most common cause of dementia in patients over 55. Over the course of this disease, patients suffer progressive impairment in higher cognitive functioning, including memory loss, spatial disorientation, language deficits, and mood and behavior changes. In end-stage AD, patients become rigid, mute, and bedridden. Definitive diagnosis of AD requires histological examination of the brain; however, with proficient clinical evaluation postmortem findings agree with clinical diagnosis in approximately 90% of cases. Grossly, brains affected by AD demonstrate cortical atrophy with widening of the sulci; changes are usually most pronounced in the frontal, temporal, and parietal lobes. With advanced disease, parenchymal atrophy results in compensatory dilation of the ventricles (hydrocephalus ex vacuo). The most severe pathology is found in the hippocampus and the nucleus basalis of Meynert of the anterior forebrain, which represent the main source of cholinergic input to the cerebral cortex. The characteristic microscopic lesions in AD are neuritic plaques and NFTs. Plaques consist of focal, spherical deposits of aggregated amyloid beta (A) fibrils surrounded by degenerating neuronal processes

(dystrophic neuritis), reactive astrocytes and microglia; A plays a major role in the pathogenesis of AD. NFTs represent twisted bundles of filaments within neuronal cell bodies that extend into dendrites. Their chief constituent is a hyperphosphorylated tau protein, an axonal microtubuleassociated protein important for proper assembly and stability of microtubules, which are involved in the transport of essential molecules through the neuron. NFTs are also seen in neurodegenerative diseases other than AD. They are well demonstrated with silver stain and particularly affect pyramidal neurons (e.g., frontal cortex, hippocampus, amygdala) where they often have an elongated, flame-shaped appearance. Choice B refers to injury caused by thiamine deficiency in alcoholism; choice C describes the morphological appearance of a glioblastoma; choice D reflects changes seen in multiple sclerosis, and choice E describes biochemical changes that occur in cerebral ischemia.

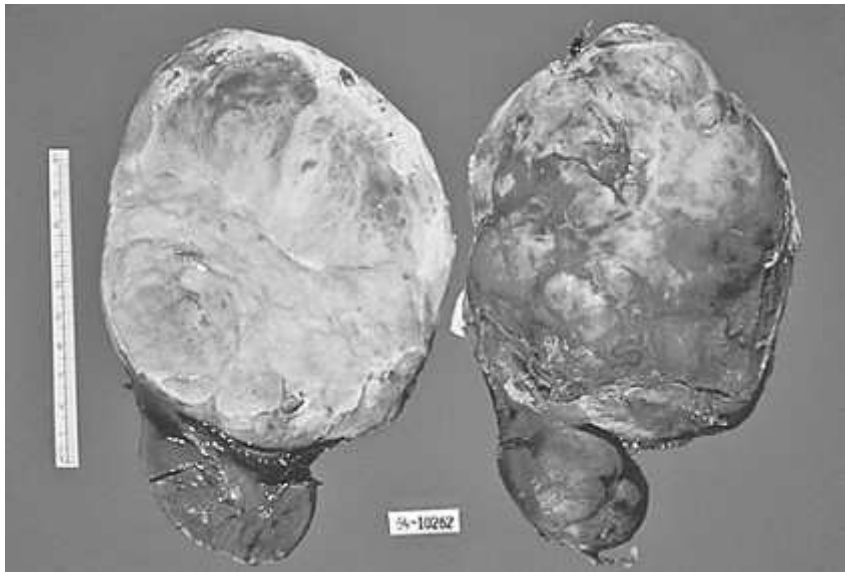
QUESTION 523
A 33-year-old man comes to see you because of several episodes of hemoptysis and dyspnea during the last 2 weeks. Physical examination reveals hypertension and edema. You order some laboratory tests and the results indicate an iron-deficiency anemia, hematuria, and proteinuria with RBC casts. At this point you strongly suspect that he has which of the following diseases?

A. fibrosing alveolitis
B. Goodpasture syndrome
C. Kartagener syndrome
D. systemic lupus erythematosus
E. Wegener granulomatosis

Correct Answer: B
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Goodpasture syndrome consists of antibodies against basement membrane material, recurrent pulmonary hemorrhage, and glomerulonephritis. The pathologic changes are due to a type II hypersensitivity reaction along the basement membranes of the lung and kidney. Steroids, plasmapheresis, and immunosuppressive medicines may help in a minority of cases. Fibrosing alveolitis (choice A) is a pulmonary disorder of unknown etiology. Glomerulonephritis and pulmonary hemorrhage are not observed clinically. Kartagener syndrome (choice C) is a hereditary disease of infancy due to a defect in respiratory ciliary action. Systemic lupus erythematosus (choice D) may present with renal insufficiency. Antibodies are directed against nuclear antigens. Wegener granulomatosis (choice E) may present clinically with pulmonary hemorrhages and renal insufficiency. There are antibodies against neutrophil components, not basement membrane material.

QUESTION 524
During a routine pediatric visit, you discover a large abdominal mass in a 2-year-old boy. The mass is surgically removed and is illustrated in below figure. What is the most likely diagnosis?



A. abscess
B. neuroblastoma
C. renal cell carcinoma
D. tuberculosis
E. Wilms' tumor

Correct Answer: E
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Figure shows a large tumor mass originating in the kidney. Wilms' tumor (or nephroblastoma) is the most common primary renal tumor of childhood and the second most common malignancy overall after lymphoma/ leukemia. It typically presents as a large abdominal mass discovered by a parent. An abscess (choice A) is a localized collection of pus that is not compatible with the solid mass shown here. A neuroblastoma (choice B) is most commonly primary in the adrenal and is unlikely to arise in the kidney. Renal cell carcinoma (choice C) is the most common primary renal tumor in adults, but is not expected in a child. Tuberculosis (choice D) would be identified by caseous necrosis, which has the appearance of amorphous crumbled cheese, not the solid appearance shown here.

QUESTION 525
A 28-year-old woman with no significant past medical history presents to her primary care physician complaining of a chronic productive cough with blood-tinged

sputum, night sweats, low-grade fever, and a 15-lbs weight loss over the past 6 weeks. Chest x-ray reveals a cavitary lesion in the left upper lobe and a calcified left hilar lymph node. Biopsy of the left upper lobe mass would most likely demonstrate which of the following?

A. amorphous eosinophilic material surrounded by epithelioid cells and T-lymphocytes
B. disorganized pleomorphic and hyperchromatic cells with rare mitotic figures
C. numerous neutrophils and necrotic debris surrounded by a fibrous capsule
D. scattered macrophages interspersed with regenerating alveolar cells and sparse collagen deposition
E. sheets of small, uniform basophilic cells with large nuclei and scant cytoplasm

Correct Answer: A
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
This clinical scenario describes secondary tuberculosis (TB). Upon initial exposure to the bacillus, an individual develops primary TB, where M. tuberculosis is phagocytosed by alveolar macrophages and transported to the hilar lymph nodes. As naïve macrophages are unable to kill the mycobacterium, bacteria multiply and lyse the host cell, at which time they infect other macrophages. T-cell immunity develops after a few weeks to control the initial infection. An epithelioid-cell granulomatous inflammation occurs at the site of original parenchymal infection, which, upon healing, results in scar formation, at times with late calcification that may leave a residual lesion potentially visible on chest x- ray. This parenchymal scar in association with an enlarged (and possibly calcified) hilar lymph node is known as the Ghon complex. In approximately 9095% of immunocompetent individuals, complete healing occurs. Because M. tuberculosis may persist within macrophages for many years, reactivation may occur, although the mechanisms responsible for keeping the bacilli dormant as well as those leading to reactivation are unknown. Reactivation (or, on less frequent occasions, reinfection) of TB is known as secondary TB. Typical clinical symptoms include weight loss, low-grade fever, and drenching night sweats. Reactivated TB has a predilection for the upper lung zones, presumably due to the greater availability of oxygen in this area, which enhances multiplication of the aerobic bacilli. An enhanced delayed hypersensitivity reaction results in an amplified local inflammatory response with extensive caseous necrosis. Multiple, small granulomas coalesce to form a large solid mass of fibrocaseous granulomatous inflammation known as a tuberculoma. Caseous necrosis undergoes liquefaction, and with extension of disease may erode into a bronchus, which leads to cavitation of the tuberculoma and coughing up of infectious, potentially bloody sputum. Microscopically, granulomatous inflammation is demonstrated by a central area of amorphous, eosinophilic material surrounded by epithelioid cells, frequently with Langhans-type giant cells, and an outer rim of predominantly T-lymphocytes. Disorganized pleomorphic and hyperchromatic cells with rare mitotic figures (choice B) is a generic description for lung carcinoma. Numerous neutrophils and necrotic debris surrounded by a fibrous capsule (choice C) would be suggestive of a chronic abscess, while scattered macrophages interspersed with regenerating alveolar cells and sparse collagen deposition (choice D) would occur following a necrotizing lung infection (e.g., S. aureus). Sheets of small, uniform basophilic cells with large nuclei and scant cytoplasm (choice E) is the morphological description of undifferentiated small cell (oat cell) lung carcinoma.

QUESTION 526
A 22-year-old man is evaluated for repeated episodes of pulmonary infections, including a recent one that is productive of foul, purulent sputum, accompanied by shortness of breath. Past medical history is also significant for chronic sinus infections with mucopurulent discharge. Physical examination is remarkable for scattered rhonchi and rales throughout all lung fields. Imaging studies show abnormally dilated and thickened airways extending close to the pleural surface and a cardiac silhouette in the right thorax. Bronchoscopy demonstrates numerous mucopurulent plugs. Which of the following is most likely responsible for these changes?

A. abnormal neutrophilic function resulting in impaired degranulation
B. alpha-1 antiprotease deficiency (PiZZ phenotype)
C. cell membrane defect resulting in abnormally viscous glandular secretions
D. defect in ciliary motility due to the absence of dynein arms
E. hypersensitivity reaction associated with c-ANCA and granuloma formation

Correct Answer: D
Section: Pathology and Path physiology
Explanation

Explanation/Reference:
Explanation:
Kartagener syndrome is defined by the triad of bronchiectasis, sinusitis, and situs inversus that, in this patient, were apparent from the foul sputum, history of sinusitis, and location of the heart in the right chest. The cause of this syndrome is the lack of ciliary motility leading to poor clearing of the respiratory tract and susceptibility to infections. During embryogenesis, cilia assist with cell migration and the situs inversus is most probably the result of their lack of function. Abnormal neutrophilic function resulting in impaired degranulation (choice A) has been observed in different conditions including in HIV-infected patients but this cannot explain the situs inversus. Alpha-1 antiprotease deficiency (PiZZ phenotype) (choice B) is a cause of emphysema and liver cirrhosis, but is not associated with the findings in this patient. Cell membrane defect resulting in abnormally viscous glandular secretions (choice C) is a description of cystic fibrosis that is associated, among other things, with recurrent lung infections but not situs inversus. Hypersensitivity disease associated with c-ANCA and granuloma formation (choice E) is a description of Wegener granulomatosis which is associated with lung infections and sinusitis, but once again has no association with situs inversus.

QUESTION 527
Which of the following drugs acts primarily on an intracellular receptor?

A. abciximab
B. dexamethasone
C. insulin
D. propranolol
E. salmeterol

Correct Answer: B
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Dexamethasone, a corticosteroid, combines with a cytoplasmic steroid receptor, enters the nucleus, and alters gene expression. The other agents listed (choices A, CE) act on membrane receptors.

QUESTION 528
Which of the following receptor types is associated with the most rapid response time?

A. G-protein-coupled receptors (e.g., muscarinic receptors)
B. ion channel receptors (e.g., nicotinic receptors)
C. Jak-STAT receptors (e.g., for cytokines)
D. steroid receptors (e.g., for corticosteroids)
E. transmembrane enzyme receptors (e.g., for insulin)

Correct Answer: B
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Response times for ion channel receptors are measured in milliseconds, for G proteincoupled receptors (choice A), transmembrane enzyme receptors (choice E), and Jak-STAT receptors (choice C) in seconds to minutes, and for steroid receptors (choice D) in hours or days.

QUESTION 529
Which of the following responses to sympathetic nerve discharge is mediated at the effector cell by acetylcholine?

A. decreased blood flow in the skin
B. increased blood fatty acids
C. increased blood glucose
D. increased heart rate
E. increased sweating

Correct Answer: E
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Thermoregulatory sweating is mediated by muscarinic receptors and is induced by the release of acetylcholine from cholinergic sympathetic nerve fibers. Therefore, sympathetic sweating can be mimicked by administration of muscarinic agonists such as bethanechol. Choices A through D are effects mediated by alpha- (choice A) or beta adrenoreceptors (choices B, C, D).

QUESTION 530
Which of the following drugs inhibit osteoclastic activity more than osteoblastic activity and have been beneficial in osteoporosis, hypercalcemia of malignancy, and Paget disease?

A. alendronate
B. calcitonin
C. fluoride
D. parathyroid hormone
E. vitamin D

Correct Answer: A
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Alendronate is a bisphosphonate, the class of drugs that has proved most effective in the treatment and prevention of osteoporosis. This class of drug is also useful in the management of hypercalcemia and certain neoplasms. Calcitonin (choice B) has been shown to slow bone loss in postmenopausal women and to treat postoperative pancreatitis. Fluoride (choice C) is used primarily in the prevention of dental caries. Parathyroid hormone (choice D), marketed as Forteo, is currently used in the clinic to treat osteoporosis. Vitamin D (choice E) has shown benefit in increasing bone deposition in osteoporotic patients. However, choices BE do not have clinical use in the treatment of malignancy or Paget disease.

QUESTION 531
The location of the lesion in Horner syndrome (either preganglionic or postganglionic) can be determined by the use of certain sympathomimetics. Which of the following agents would distinguish between a preganglionic versus a postganglionic lesion?

A. amphetamine
B. atenolol
C. epinephrine
D. isoproterenol
E. phenylephrine

Correct Answer: A
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Indirectly acting sympathomimetics (e.g., amphetamines, cocaine) are useful in this situation because their action requires the presence of intact postganglionic noradrenergic neurons. Thus administration of hydroxyamphetamine into the eye will cause mydriasis in a Horner patient if the lesion is preganglionic (postganglionic neuron intact), but not if the lesion is postganglionic. In contrast, directacting sympathomimetics (choices C, D, E) will have the same effect regardless of the location of the lesion. Beta antagonists (choice B) will not produce any effect on the pupil.

QUESTION 532
Mifepristone has antagonist action at which of the following receptors?

A. beta adrenoceptors
B. dopamine receptors
C. insulin receptors
D. low-density lipoprotein receptors
E. progesterone receptors

Correct Answer: E
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Mifepristone, also known as RU 486, is an effective antagonist at progesterone and glucocorticoid receptors. It has no effect on the other receptors listed (choices AD).

QUESTION 533
A 50-year-old man presents with a blood pressure of 160/100. He is to be started on hydrochlorothiazide. Which of the following is a common adverse effect of hydrochlorothiazide?

A. atrioventricular (AV) blockade
B. constipation
C. drug-induced lupus erythematosus
D. potassium wasting
E. tachycardia

Correct Answer: D
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Because thiazides decrease the reabsorption of sodium in the distal convoluted tubule, aldosterone secretion is increased and a compensatory response is evoked that releases potassium in response to increased sodium reabsorption in the cortical collecting tubule, therefore, potassium- wasting results. Other adverse effects of thiazides include increased blood glucose, uric acid, and lipids. None of the other choices (AB, E) are adverse effects of thiazide administration.

QUESTION 534
A 57-year-old man presents with angina. He uses 1 or 2 nitroglycerin tables sublingually when he experiences chest pain. Which of the following drugs may interact to cause serious hypotension if taken 6 hours or less before the nitrate?

A. clonidine
B. diltiazem
C. metronidazole
D. phentolamine
E. sildenafil

Correct Answer: E
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Nitrates release nitric oxide in smooth muscle and cause relaxation by facilitating the production of cGMP. Sildenafil (and related drugs for erectile dysfunction, tadalafil and vardenafil) inhibit the inactivation of cGMP. When sildenafil and a nitrate are combined, excessive amounts of cGMP accumulate and may cause severe hypotension. The other drugs listed (choices Athrough D) have no significant interactions with nitrates.

QUESTION 535
Diltiazem as used in angina pectoris has several beneficial actions that contribute to the prevention of the anginal symptoms. Which of the following actions is detrimental in angina?

A. reduced arterial blood pressure
B. increased diastolic heart size
C. reduced systolic myocardial fiber tension
D. bradycardia
E. slowed AV conduction

Correct Answer: B
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Calcium channel blockers cause a decrease in arterial pressure, heart rate, and cardiac contractility, all of which help to reduce myocardial oxygen requirement and thereby reduce angina pain. However, the reduction in contractility increases diastolic cardiac size, which increases oxygen requirement and is therefore detrimental. The other effects listed (choices A, C, and E) are all valid beneficial actions of calcium blockers in angina. Slowed AV conduction E. occurs, but is of no significance in angina.

QUESTION 536
Which of the following beta-lactam drugs has good activity against beta-lactamase-producing organisms and penetrates readily into cerebrospinal fluid?

A. amoxicillin
B. cefazolin
C. clavulanic acid
D. imipenem
E. ticarcillin

Correct Answer: D
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Imipenem is the only drug listed that is effective against many beta-lactamase-producing organisms and penetrate the bloodbrain barrier. Clavulanic acid C. is an inhibitor of beta lactamase and is used with an antibiotic but is not an antibiotic itself. None of the other drugs (choices A, B, D, and E) readily penetrate in the cerebrospinal fluid.

QUESTION 537
A 73-year-old patient has heart failure that has worsened over the past 12 months. Which of the following drugs is likely to slow progression even though it has no direct positive or negative effects on cardiac contractility?

A. digoxin
B. dobutamine
C. losartan
D. nesiritide

E. propranolol

Correct Answer: C
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Losartan, an AT1 angiotensin receptor antagonist, has been shown to slow the progression of heart failure, in common with the ACE inhibitors, beta blockers, and spironolactone, which also slow progression of this disease. Positive inotropic agents such as digoxin (choice A) and dobutamine (choice B) do not slow progression although they may be useful for reducing symptoms. Nesiritide (choice D) is a peptide that causes vasodilation and sodium diuresis and may have value in acute but not chronic failure. Propranolol (choice E) probably slows progression of heart failure but it has direct negative inotropic effects on the heart.

QUESTION 538
Antiarrhythmic drugs have a variety of adverse effects that must be monitored carefully. Which of the following drugs is associated with discoloration of the skin, photosensitivity, thyroid dysfunction, and pulmonary complications?

A. amiodarone
B. diltiazem
C. ibutilide
D. lidocaine
E. procainamide

Correct Answer: A
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Amiodarone is a large, insoluble molecule that deposits in skin (and the cornea) and causes photosensitivity. It contains two iodine atoms, which may be responsible for binding to thyroid receptors and the observed thyroid problems. It is associated with pulmonary fibrosis (sometimes fatal), but the mechanism is unknown. In spite of these adverse effects, it is extremely useful in arrhythmia treatment. Diltiazem (choice B) is associated with constipation and cardiac depression; ibutilide (choice C) with torsade de pointe arrhythmia, lidocaine (choice D) with convulsions, and procainamide (choice E) with torsade de pointe arrhythmia and drug-induced lupus.

QUESTION 539
Which of the following drugs causes hyperchloremic metabolic acidosis and may cause hyperammonemia in a patient with cirrhosis?

A. acetazolamide
B. amiloride

C. furosemide
D. hydrochlorothiazide
E. spironolactone

Correct Answer: A
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Acetazolamide acts in the proximal tubule to block carbonic anhydrase, greatly increasing bicarbonate excretion and alkalinizing the urine while causing metabolic acidosis. In cirrhosis, ammonia is excreted in larger amounts because urea production in the liver is limited. If an acid urine (necessary for converting ammonia to ammonium ion) cannot be produced, the ammonia is promptly reabsorbed, causing hyperammonemia and hepatic encephalopathy. None of the other drugs (choices BE) causes hyperammonemia in cirrhotic patients.

QUESTION 540
Serotonin (5-HT) is one of several mediators of the signs and symptoms of carcinoid tumor. When released from this neoplasm, most of the manifestations of 5-HT are the result of activation of the 5-H receptor. These manifestations are therefore likely to include which of the following effects?

T_2

A. bronchospasm
B. constipation
C. skeletal muscle weakness
D. tachycardia
E. ulceration of the stomach or duodenum

Correct Answer: A
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
5-H receptors mediate smooth muscle contraction and thus cause bronchospasm and diarrhea, not

T_2

constipation (choice B). Skeletal muscle (choice C) and cardiac muscle (choice D) are relatively insensitive to 5-HT. Peptic ulceration (choice E) is not mediated in part by 5-HT; the autacoid actually reduces acid secretion.

QUESTION 541
Which of the following drugs is useful in asthma because it stabilizes mast cells?

A. albuterol
B. cromolyn
C. ipratropium
D. salmeterol
E. theophylline

Correct Answer: B
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Cromolyn is a prophylactic agent for asthma that appears to stabilize mast cells. Albuterol A. is a shorter acting beta-2-selective agonist that is used for acute, not prophylactic, therapy. Ipratropium (choice C) is an antimuscarinic drug. Salmeterol D. has a long duration beta-2-agonist action that appears to have an anti-inflammatory action and is useful in prophylaxis of asthmatic attacks. It has a slow onset of action that makes it useless in treating acute attacks. Theophylline (choice E) is an intermediate duration agent that acts by inhibition of phosphodiesterase or adenosine receptors.

QUESTION 542
Zolpidem is a newer sedative-hypnotic drug approved for use as a sleeping pill. Which of the following statements describes the major difference between zolpidem and older hypnotics such as barbiturates and benzodiazepines?

A. associated with thrombocytopenia
B. does not act on chloride channels in the CNS
C. has significant anticonvulsant activity
D. much longer duration of action
E. reduced addiction liability

Correct Answer: E
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Zolpidem has greatly reduced addiction liability compared to barbiturates and benzodiazepines even though it does act on chloride channels (choice B). Zolpidem does not have major anticonvulsant actions (choice C), a longer duration of action (choice D), or thrombocytopenic toxicity (choice A).

QUESTION 543
A child with absence seizures is being evaluated for therapy with ethosuximide. Which of the following is the most common adverse effect of ethosuximide in children?

A. hemolytic anemia
B. excessive sedation
C. hepatic necrosis
D. nephropathy
E. torsade de pointe arrhythmia

Correct Answer: B
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Ethosuximide is usually a very safe drug, but can cause significant sedation. Aplastic anemia but not hemolytic anemia (choice A) has rarely been associated with the use of ethosuximide, and with carbamazepine and felbamate. Hepatotoxicity (choice C) is a rare but potentially lethal adverse effect of valproic acid that occurs most commonly in children under the age of 2 and those taking multiple drugs. Authorities recommend monitoring liver function tests when starting this drug. Nephropathy (choice D) is not usually reported with antiseizure drugs. Torsade de pointe arrhythmia (choice E) has not occurred with significant frequency during use of anticonvulsant drugs.

QUESTION 544
A 70-year-old man presents with Parkinson's disease in an early stage. Which of the following drugs acts directly on dopamine receptors to reduce the signs and symptoms of Parkinson's disease?

A. amantadine
B. carbidopa
C. entacapone
D. orphenadrine
E. pramipexole

Correct Answer: E
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:

Pramipexole is a dopamine receptor agonist unrelated to levodopa or ergot derivatives such as bromocriptine and pergolide (which are also useful dopamine agonists). Amantadine (choice A) acts to facilitate the release or slow the reuptake of dopamine, but does not act on the dopamine receptor. Carbidopa (choice B) blocks the peripheral conversion of levodopa to dopamine, it does not act on dopamine receptors. Entacapone (choice C) blocks the peripheral metabolism of levodopa by catechol- O-methyltransferase. Orphenadrine (choice D) is a centrally acting anticholinergic agent that is sometimes used in Parkinson's disease.

QUESTION 545
Which of the following agents used in general anesthesia is least likely to cause postoperative nausea and vomiting?

A. enflurane
B. etomidate
C. isoflurane
D. morphine
E. propofol

Correct Answer: E
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Propofol may reduce blood pressure through vasodilating and negative inotropic effects on the heart, but is notable for rapid recovery and its freedom from postoperative nausea and vomiting. For this reason, it is extremely popular for day surgery. None of the other anesthetics (choices AD) are free from causing postoperative nausea.

QUESTION 546
Which of the following is the only local anesthetic that causes vasoconstriction and may result in an increase in blood pressure?

A. bupivacaine
B. cocaine
C. etidocaine
D. lidocaine
E. tetracaine

Correct Answer: B
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:

Cocaine is the only local anesthetic that causes sympathomimetic effects (by inhibiting reuptake of norepinephrine into sympathetic nerve endings); it therefore regularly causes local vasoconstriction and may increase blood pressure. All the other local anesthetics (choices A, CE) cause vasodilation and lower blood pressure.

QUESTION 547
A 26-year-old woman with cerebral palsy complains of severe pain associated with spasms in her leg muscles. Which of the following drugs is used in cerebral palsy to reduce skeletal muscle spasticity by an action on cholinergic nerve endings?

A. baclofen
B. botulinum toxin
C. dantrolene
D. diazepam
E. tubocurarine

Correct Answer: B
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Botulinum toxin acts on cholinergic nerve endings (including skeletal muscle motor nerve endings) to reduce acetylcholine release. Baclofen A. acts in the CNS to activate GAB receptors; some

A_B

sedation may result. Dantrolene C. acts within the skeletal muscle cell to reduce calcium release from the sarcoplasmic reticulum; reduction of muscle spasm results without central nervous system depression. Diazepam (choice D) facilitates GABAergic transmission in the brain and spinal cord; it does not act on cholinergic transmission. Tubocurarine (choice E) causes profound skeletal muscle paralysis by blocking acetylcholine receptors in the neuromuscular junction. Unlike the other drugs listed, it is not useful in cerebral palsy.

QUESTION 548
A 35-year-old man has severe schizophrenia. He is institutionalized and maintained on antipsychotic medication. Which of the following drugs is most likely to cause parkinsonian adverse effects?

A. clozapine
B. fluphenazine
C. haloperidol
D. olanzapine
E. quetiapine

Correct Answer: C
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Haloperidol is a very potent and efficacious antipsychotic but also manifests the highest incidence of extrapyramidal effects. Clozapine (choice A), olanzapine (choice D), and quetiapine (choice E) are newer, atypical antipsychotic agents with much lower incidence of extrapyramidal toxicity. Fluphenazine (choice B) is a potent phenothiazine with an intermediate tendency to produce parkinson- like effects.

QUESTION 549
Which of the following drugs is most dangerous in suicidal overdosage?

A. bupropion
B. citalopram
C. fluoxetine
D. imipramine
E. phenelzine

Correct Answer: D
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Imipramine and other tricyclics are the most dangerous antidepressants when taken in overdosage because of their cardiotoxic (arrhythmias) and neurologic (seizures) effects. Bupropion (choice A), the selective serotonin reuptake inhibitors (SSRIs) (choices B and C), and MAO inhibitors (choice E) are considerably less dangerous.

QUESTION 550
Apatient has been treated for bipolar disorder for several months. Which of the following is a common adverse effect of lithium carbonate?

A. dry mouth
B. hyperthyroidism
C. leucopenia
D. nephrogenic diabetes insipidus
E. parkinsonian extrapyramidal symptoms

Correct Answer: D
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Nephrogenic diabetes insipidus is a common adverse effect of lithium at therapeutic dosage. Dry mouth (choice A) and other anticholinergic toxicities are common with tricyclic antidepressants and some phenothiazines. Lithium may induce hypothyroidism, but not hyperthyroidism (choice B). Similarly, lithium increases rather than decreases white blood cell count (choice C). Finally, lithium often causes tremor, but not parkinsonism (choice E).

QUESTION 551
Methadone has been used in opioid addiction maintenance clinics with partial success. Its ability to reduce the use of heroin and morphine by recovering addicts can be ascribed to which of the following mechanisms?

A. agonist effects at central dopamine receptors
B. antidepressant effects at serotonin (5-HT) receptors
C. antagonist actions at the mu opioid receptor
D. blockade of the metabolic activation of heroin and morphine to their active forms
E. long-lasting saturation of the mu opioid receptor and development of tolerance

Correct Answer: E
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Methadone is a typical strong agonist at opioid mu receptors and differs from morphine chiefly in its long duration of binding to the receptor and long elimination half-life. It therefore produces a prolonged opioid effect that causes tolerance to the euphoric action of short-acting heroin and morphine. Methadone has no opioid antagonist action (choice C), nor does it act on metabolic pathways (choice D), serotonin receptors (choice B), or dopamine receptors (choice E).

QUESTION 552
Which of the following drugs has opioid antagonist actions and also reduces nicotine and alcohol craving in persons dependent on those drugs?

A. bupropion
B. flumazenil
C. nalbuphine
D. naloxone
E. naltrexone

Correct Answer: E
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Naltrexone is a very long-acting opioid antagonist that has also been shown to reduce craving and dependence in smokers and alcoholics. The mechanisms for the latter effects are not fully understood. Bupropion (choice A) is an antidepressant that has some efficacy in tobacco dependence. It is not an opioid antagonist. Flumazenil (choice B) is a benzodiazepine antagonist that is useful in BDZ overdose. It has no opioid antagonist effect. Nalbuphine (choice C) is an opioid partial agonist that has analgesic effects but can also antagonize the actions of strong agonists like morphine. Naloxone (choice D) is a shortacting opioid antagonist but has not been shown to have efficacy in tobacco or alcohol dependence.

QUESTION 553
A known drug abuser is brought to the emergency room by the police. He is in restraints, combative, and hallucinating. His blood pressure, heart rate, and body temperature are elevated. Pupils are dilated and demonstrate both horizontal and vertical nystagmus. Which of the following drugs would cause this presentation?

A. amphetamine
B. heroin
C. LSD
D. phencyclidine
E. scopolamine

Correct Answer: D
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Phencyclidine, an NMDA receptor antagonist, is a more violent hallucinogen than most other drugs in this class (LSD, mescaline, scopolamine). It causes sympathetic discharge and muscle twitching; nystagmus is very common. Amphetamine (choice A) is a sympathomimetic stimulant that can produce hallucinations or toxic psychosis in overdose, but is not usually associated with nystagmus. Heroin (choice B) is a depressant drug and does not present with combative stimulation. Pupils are constricted by opioids. LSD (choice C) is a classical hallucinogen, but does not commonly cause combativeness or nystagmus. Scopolamine (choice E) similarly does not usually cause combativeness or nystagmus.
Both LSD and scopolamine cause mydriasis.

QUESTION 554
Which of the following enzymes is inhibited by drugs of the class to which amoxicillin belongs?

A. alanine racemase
B. beta lactamase

C. enolpyruvate transferase
D. transglycosylase
E. transpeptidase

Correct Answer: E
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
All of the beta-lactam antibiotics (penicillins, cephalosporins, carbapenems, monobactams) inhibit one of the final steps in the synthesis of the bacterial cell wall, cross-linking of peptidoglycan chains by transpeptidase. Alanine racemase (choice A) is inhibited by cycloserine, which is used in the treatment of M. tuberculosis. Beta lactamase (choice B) is inhibited by drugs (e.g., clavulanic acid, sulbactam, tazobactam) used to prevent resistance by bacteria that possess it. Enolpyruvate transferase (choice C) is inhibited by fosfomycin, which is used for urinary tract infections. Transglycosylase (choice D), another enzyme important in cell wall cross linking, is inhibited by vancomycin.

QUESTION 555
Which of the following drugs is selectively antifungal because of the difference between cholesterol (in mammalian cell membranes) and ergosterol (in fungal membranes)?

A. amphotericin B
B. caspofungin
C. fluconazole
D. griseofulvin
E. terbinafine

Correct Answer: A
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Amphotericin B binds selectively to ergosterol and forms artificial pores in fungal membranes. These pores result in loss of homeostasis and death of the fungal cell. Caspofungin (choice B) is a member of the echinocandins, the newest antifungal antibiotics. These agents disrupt the fungal cell wall by inhibiting the synthesis of beta(1-3) glucan. Fluconazole (choice C) and other azoles (ketoconazole, itraconazole, voriconazole, posaconazole) inhibit ergosterol synthesis. Griseofulvin (choice D) interferes with microtubule function and cell division in fungi. Terbinafine (choice E) inhibits squalene epoxidase in fungi and reduces ergosterol synthesis.

QUESTION 556
Which of the following antifungal drugs is strongly associated with drug interactions resulting from inhibition of CYP 3A4?

A. amphotericin B
B. caspofungin
C. fluconazole
D. ketoconazole
E. flucytosine

Correct Answer: D
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Ketoconazole is a potent inhibitor of the cytochrome P450 enzyme, CYP 3A4. Because CYP 3A4 is involved in the metabolism of almost 50% of the drugs in use, ketoconazole is implicated in many pharmacokinetic drug interactions. Amphotericin B (choice A) causes nephrotoxicity and may therefore interfere with the excretion of other drugs. Caspofungin (choice B) appears to be free of most drug interactions. Fluconazole (choice C), although a member of the same (azole) group as ketoconazole, is much less potent as a CYP 3A4 inhibitor and is associated with far fewer drug interactions. Flucytosine (choice E) is associated with few pharmacokinetic drug interactions, but by metabolism to fluorouracil it is toxic to the bone marrow and other rapidly dividing cells.

QUESTION 557
Which of the following is useful in rheumatoid arthritis because it binds tumor necrosis factoralpha (TNF-alpha)?

A. leflunomide
B. infliximab
C. methotrexate
D. paclitaxel
E. trastuzumab

Correct Answer: B
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Infliximab is a chimeric monoclonal antibody that binds TNF-alpha and is useful in rheumatoid arthritis, ulcerative colitis, and several other immune diseases. Leflunomide (choice A) inhibits ribonucleotide synthesis and thereby reduces T-cell proliferation. Methotrexate (choice C) is an antimetabolite that inhibits cell proliferation. It is useful in rheumatoid arthritis. Paclitaxel (choice D) is a microtubule-binding agent that is cytotoxic in certain neoplasms and slows restenosis in coronary stents. It is not used in autoimmune diseases. Trastuzumab (choice E) is an antibody to the human epidermal growth factor receptor and is useful in metastatic breast cancer.

QUESTION 558
Which of the following agents used to prevent organ transplant rejection is most likely to cause significant decrease in creatinine clearance?

A. antilymphocyte globulin
B. cyclosporine
C. mycophenolate mofetil
D. prednisone
E. sirolimus

Correct Answer: B
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Cyclosporine and tacrolimus (not listed) are associated with nephrotoxicity as a major adverse effect. Antilymphocyte globulin (choice A) is associated with foreign protein reactions, including anaphylaxis. Mycophenolate mofetil (choice C) causes GI disturbances and myelosuppression. Prednisone (choice D) causes a variety of chronic toxicities conveniently summarized as "Cushingoid effects" but has little acute toxicity. Sirolimus (choice E) is associated with bone marrow suppression.

QUESTION 559
Which of the following antidiabetic agents acts on the peroxisome proliferator-activated receptor- gamma (PPAR-gamma) nuclear receptor?

A. acarbose
B. glyburide
C. insulin lispro
D. metformin
E. pioglitazone

Correct Answer: E
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
The glitazone drugs (pioglitazone, rosiglitazone) reduce insulin resistance in peripheral tissues by activating the PPAR-gamma receptor, which promotes glucose uptake and utilization. Acarbose (choice A) interferes with the action of intestinal alpha-glucosidases and reduces absorption of glucose. Glyburide (choice B) and other sulfonylurea hypoglycemic drugs block the ATP-activated potassium channel in pancreatic cells and cause increased insulin release. Insulin lispro (choice C) is a modified insulin with rapid onset and offset of action. All insulins act by causing insertion of glucose transporters into cell membranes and several other

mechanisms. The mechanism of action of metformin (choice D) and similar biguanide antidiabetic drugs is still unclear but may involve reduction of glucagon release, stimulation of glycolysis in peripheral tissues, or decreased hepatic and renal gluconeogenesis.

QUESTION 560
Exhibit:

A. iodine uptake by the thyroid
B. organification of iodine in the thyroid
C. peripheral conversion of T_4 to T_3
D. peripheral thyroxine (T_4) and T_3 receptors
E. thyroglobulin proteolysis

Please refer to the exhibit.
Which of the following mechanisms most accurately describes the blocking action of methimazole?

A. A
B. B
C. C
D. D
E. E

Correct Answer: B
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Methimazole (and other thioamides) act primarily by inhibiting thyroid peroxidase, the critical enzyme in iodine organification. They also inhibit coupling of iodotyrosines in thyroglobulin. They do not block iodine uptake by the gland. Block of iodine uptake by the thyroid (choice A) is a property of antithyroid anions such as thiocyanate (SC) and perchlorate (Cl). Inhibition of peripheral

N^-

conversion of to (choice C) is the mechanism of beta blockers and iodine-containing radio-

T_4

opaque drugs such as ipodate. Block of peripheral thyroid receptors (choice D) is not a mechanism of any currently available drug. Block of thyroglobulin proteolysis and reduced release of thyroxine from the gland (choice E) is a property of iodide ion.

QUESTION 561
Which of the following adverse effects of chronic high-dose prednisone administration represents a mineralocorticoid effect?

A. buffalo hump
B. easy bruising
C. edema
D. moon facies
E. psychosis

Correct Answer: C
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Edema and hypertension will occur with any corticosteroid that has mineralocoid properties if given in high dosage over a long period. Prednisone, though much less potent than cortisol as a mineralocorticoid, retains some salt-retaining potency. Newer glucocorticoids, such as dexamethasone and triamcinolone, are much less likely to retain salt and water. Buffalo hump (choice A) and moon facies (choice D) reflect the fat metabolism effects of glucocorticoid activity. Easy bruising (choice B) and striae reflect the catabolic action of glucocorticoids on proteins. The mechanism of central nervous system dysfunction (choice E) is not understood, but it is associated with glucocorticoid, not mineralocorticoid, activity.

QUESTION 562
Which of the following drugs is used to accelerate pulmonary maturation in the fetus in women with premature labor?

A. aminoglutethimide
B. betamethasone
C. mifepristone
D. misoprostol
E. prostacyclin

Correct Answer: B
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Glucocorticoids help accelerate maturation of the lungs in the fetus at the end of term. In preterm labor, these drugs help prevent respiratory failure in the newborn. Betamethasone is the preferred corticosteroid for this purpose because it is poorly bound in the maternal serum and transfers into the fetal circulation more readily. The other drugs listed (choices A, CE) are of no value in this setting.

QUESTION 563
The increased risk of blood clots in women who use certain combined estrogen/progestin birth control pills is well established. Which of the following best explains this association?

A. impaired glucose tolerance
B. increased Factor II, VII, IX, and X levels produced by estrogens
C. increased plasminogen levels produced by progestins
D. increased thyroxine-binding globulin
E. increased triglyceride levels produced by progestins

Correct Answer: B
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Increased clotting factor synthesis (and decreased antithrombin III synthesis) caused by estrogens are the major factors responsible for increased incidence of thromboembolic phenomena. Glucose tolerance is impaired (choice A) in some women by progestins and would not be expected to affect clotting. Plasminogen (choice C) is increased by estrogens, not progestins, but would decrease clotting. Thyroxine-binding globulin (choice D) is also increased by estrogen, but would have little effect on clotting. Triglycerides (choice E) are increased by estrogens and would have little or no effect on clotting.

QUESTION 564
Which of the choices in the table below most accurately describes the actions of vitamin D and arathyroid hormone on calcium and phosphate in the blood?

Choice	Vitamin D		Parathyroid Hormone	
	Serum Ca^{2+}	Serum PO_4^-	Serum Ca^{2+}	Serum PO_4^-
A	↑	↑	↑	↑
B	↓	↓	↓	↓
C	↑	↑	↓	↓
D	↑	↑	↑	↓
E	↓	↓	↑	↑

A. Option A
B. Option B
C. Option C
D. Option D
E. Option E

Correct Answer: D
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Although there are several forms of vitamin D and both vitamin D and parathyroid hormone act on the intestine, kidney, and bone, the net effect of vitamin D is to increase serum calcium and phosphate, while parathyroid hormone increases serum calcium and decreases phosphate. None of the other options (choices AC, E) correctly reflects the actions of vitamin D or parathyroid hormone.

QUESTION 565
An unconscious man is brought to the emergency room. He was at home when discovered, but he works as a foreman in a chemical packaging plant. His blood pressure and heart rate are normal. He is sweating profusely, has constricted pupils, and auscultation of the lungs indicates rales and wheezing. Widespread subcutaneous muscle twitches are apparent. He has had urinary and fecal incontinence. Which of the following chemicals is the most likely cause of this poisoning?

A. isobutyl nitrite
B. metallic mercury
C. morphine

D. parathion
E. phencyclidine

Correct Answer: D
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
When a person who is exposed to chemicals in the workplace is intoxicated, both drugs of abuse and workplace exposures must be considered. The signs of this patient's intoxication match the classic picture of cholinesterase inhibitor poisoning as summarized by the mnemonic "dumbels:" diarrhea, rination, miosis, bronchospasm, excitation, lacrimation, and sweating and salivation. Isobutyl nitrite (choice A), an industrial chemical also used as a recreational drug for sex enhancement, causes tachycardia, methemoglobinemia, and signs of tissue hypoxia. Mercury (choice B) causes chemical pneumonitis and pulmonary edema. Chronic mercury exposure causes behavioral abnormalities. Morphine (choice C) causes miosis but reduces gastrointestinal activity. Phencyclidine (choice E) causes hallucinations, combativeness, and sympathetic discharge.

QUESTION 566
Which of the following drugs is considered a first-line agent in the chronic treatment of rheumatoid arthritis and in the treatment of choriocarcinoma?

A. cyclosporine
B. hydroxychloroquine
C. methotrexate
D. sulfasalazine
E. thalidomide

Correct Answer: C
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Methotrexate in very low dosage has proven effective in slowing the progression of rheumatoid arthritis and has low toxicity. It is also one of the most effective (in much higher dosage) antimetabolite cancer chemotherapeutic drugs used in choriocarcinoma. Cyclosporine (choice A) is not used in either condition but is a first-line drug in transplant immunopharmacology. Hydroxychloroquine (choice B) is a disease-modifying antirheumatoid arthritis drug, but has no efficacy in the treatment of cancer. It is more toxic and less effective in rheumatoid arthritis than methotrexate. Sulfasalazine (choice D) is also effective in slowing the progression of joint damage in rheumatoid arthritis but has no efficacy in cancer. Thalidomide (choice E) is effective in erythema nodosum leprosum and multiple myeloma but has not been demonstrated to be effective in rheumatoid arthritis or choriocarcinoma.

QUESTION 567
Which of the following drugs reduces LDL cholesterol by inhibiting an intestinal transport protein?

A. atorvastatin
B. cholestyramine
C. ezetimibe
D. gemfibrozil
E. niacin

Correct Answer: C
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Ezetimibe is an important newer drug that inhibits cholesterol and bile acid absorption from the gut by inhibiting the epithelial transport protein NPC1L1. Atorvastatin (choice A) reduces both LDL and triglycerides, but does not inhibit VLDL secretion. Cholestyramine (choice B) inhibits the reabsorption of bile acids and cholesterol from the gut and actually increases triglycerides in some patients. Gemfibrozil (choice D) activates lipoprotein lipase in peripheral tissues and reduces VLDL levels and triglycerides. It does not reduce hepatic secretion of VLDL. Niacin (choice E) is the most effective drug available for reducing triglycerides and also reduces LDL cholesterol by reducing the hepatic secretion of its precursor, VLDL particles.

QUESTION 568
Which of the following drugs corrects the anemia of pernicious anemia and prevents the neurological consequences of the disease?

A. beta-carotene
B. ferrous sulfate
C. folic acid
D. hydroxocobalamin
E. vitamin E

Correct Answer: D
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Hydroxocobalamin, is one of two forms of vitamin , the specific drug that reverses both the

B_{12}

macrocytic anemia and the neurologic defects of pernicious anemia. (Cyanocobalamin is equivalent.) Beta carotene (choice A) and vitamin E (choice E) are of no

value in anemia, nor do they reverse the neurological defects of pernicious anemia. Ferrous sulfate (choice B) is the first-line drug for the treatment of irondeficiency anemia, the most common type of anemia. It is of no value in pernicious anemia. Folic acid (choice C) is effective in reversing the anemia of vitamin deficiency, but does

B_{12}

not prevent the neurological complications of the disease.

QUESTION 569
Which of the following laxatives acts osmotically to increase the water content of the stool?

A. cascara
B. docusate
C. glycerine
D. magnesium hydroxide
E. senna

Correct Answer: D
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Magnesium hydroxide is an osmotic laxative that retains water in the lumen of the colon. Cascara (choice A) is a naturally occurring plant product that stimulates the bowel and causes evacuation within 612 hours when given orally. Docusate (choice B) is a stool-softening agent that acts entirely within the lumen. Glycerine (choice C), given by suppository, is a stool softener. Senna (choice E) is a stimulant and bulk-forming agent that increases the volume of the stool and stimulates evacuation.

QUESTION 570
Which of the following drugs binds to, and prevents disassembly of, microtubules?

A. busulfan
B. cisplatin
C. mercaptopurine
D. paclitaxel
E. vinblastine

Correct Answer: D
Section: Pharmacology

Explanation

Explanation/Reference:
Explanation:
Paclitaxel (choice D) is a plant alkaloid that interferes with microtubule disassembly. Busulfan (choice A) and cisplatin (choice B) are alkylating agents that interfere with DNAmobilization and replication. Mercaptopurine (choice C) is an antimetabolite that interferes with purine synthesis. Vinblastine (choice E) and vincristine and vinorelbine are mitotic poisons that prevent cancer cell division by interfering with microtubule assembly and thus immobilizing the mitotic spindle apparatus. Their indications and toxicities are quite different from those of paclitaxel.

QUESTION 571
Which of the following drugs blocks the action of angiotensin II at the AT1 receptor?

A. bradykinin
B. enalapril
C. losartan
D. ondansetron
E. prazosin

Correct Answer: C
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Losartan and several other drugs block the action of angiotensin II at its primary cardiovascular target, the A receptor. They are therefore useful in hypertension and heart failure. Bradykinin (choice A) is

T_1

a vasodilator peptide. It is not therapeutically useful because of undesirable side effects. Enalapril (choice B) is an ACE inhibitor and reduces the production of angiotensin II from angiotensin I. Ondansetron (choice D) is a 5-H receptor antagonist used to prevent chemotherapy-induced and

T_3

postoperative vomiting. Prazosin (choice E) is an alpha-1-selective blocker used in hypertension and benign prostatic hyperplasia.

QUESTION 572
A 73-year-old woman complains of difficulty sleeping, exercise fatigue, and shortness of breath. Examination reveals mental confusion, swollen ankles, pulmonary rales, and dyspnea while supine.
46. Chronic treatment of this patient with an angiotensin-converting enzyme (ACE) inhibitor such as captopril may be beneficial because ACE inhibitors (in addition

to other effects) are known to exert which of the following responses?

A. decrease both ventricular preload and afterload
B. increase coronary perfusion
C. increase efficiency of oxygen extraction by cardiac and skeletal muscle
D. produce a positive inotropic effect and negative chronotropic effect
E. promote ventricular remodeling and compensatory enlargement

Correct Answer: A
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
ACE inhibitors decrease ventricular preload and afterload through the inhibition of ACE and the consequent decrease in production of the pressor peptide angiotensin II, along with prolongation of the actions of the vasodilator peptide bradykinin (which is normally degraded by ACE). ACE inhibition also reduces angiotensin II-dependent augmentation of sympathetic nervous system activity. Choice B is incorrect in that ACE inhibitors exert no direct effects on coronary perfusion. Choice C is incorrect because efficiency of oxygen extraction by muscle is unaffected by ACE inhibitors. Choice D is incorrect because ACE inhibitors exert no direct effects on cardiac force or rate. Use of ACE inhibitors reduces ventricular remodeling and compensatory enlargement (choice E), a very valuable effect in heart failure.

QUESTION 573
A 73-year-old woman complains of difficulty sleeping, exercise fatigue, and shortness of breath. Examination reveals mental confusion, swollen ankles, pulmonary rales, and dyspnea while supine. Immediate treatment of the patient may be needed if signs and symptoms, especially those of pulmonary congestion, worsen rapidly. Which of the following would be most beneficial in treating acute, severe pulmonary edema?

A. amiloride
B. furosemide
C. hydrochlorothiazide
D. losartan
E. metoprolol

Correct Answer: B
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Rapid worsening of pulmonary congestion is suggestive of life-threatening acute cardiac decompensation (acute heart failure). Furosemide, a loop diuretic, is one

of the most effective agents available because it has powerful diuretic action and also reduces pulmonary vascular pressures. Amiloride (choice A) is a much less efficacious diuretic with primary action in the collecting tubule of the nephron and little or no effect on pulmonary vessels. Hydrochlorothiazide (choice C) is a diuretic of intermediate efficacy that acts in the distal convoluted tubule. Losartan (choice D) is an angiotensin receptor blocker and is not effective in acute reduction of congestive symptoms. Metoprolol (choice E) is a betaadrenoreceptor blocker that is valuable in the long-term, chronic therapy of HF, but not effective (and usually contraindicated) in acute decompensation.

QUESTION 574
Which of the following descriptions best describes the molecular mechanism underlying the therapeutic actions of the statins such as atorvastatin?

A. binding to peroxisome proliferatoractivated receptor-alpha (PPAR-alpha) resulting in stimulation of lipoprotein lipase activity
B. increased fecal excretion of bile acid resulting in increased conversion of cholesterol to bile acid
C. inhibition of hepatic cholesterol synthesis resulting in increased expression of LDL receptors
D. inhibition of hepatic VLDL secretion resulting in reduced production of IDL and LDL
E. inhibition of lecithin:cholesterol acyltransferase activity resulting in decreased conversion of IDL to LDL

Correct Answer: C
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Hepatic intracellular cholesterol levels are tightly controlled through regulation of endocytotic uptake of cholesterol within LDL particles, de novo synthesis of cholesterol, incorporation into VLDL particles, and loss due to conversion to bile acids. Inhibition of cholesterol biosynthesis through statin inhibition of the enzyme 3-hydroxymethylglutaryl- CoA reductase (HMG-CoA reductase) lowers intracellular cholesterol levels. This lowering results in increased expression of the genes for the LDL receptor and HMG-CoA reductase. Increased expression of LDL receptors leads to increased endocytic uptake of LDL particles from the blood and consequent reduction of circulating levels of LDL cholesterol. Choice D is incorrect because the statins do not affect hepatic VLDL secretion. Inhibition of VLDL secretion is probably the mechanism of action for nicotinic acid in lowering VLDL and LDL. Choice E is incorrect because the statins do not affect lecithin:cholesterol acyltransferase (LCAT) activity. Binding to PPAR-alpha and activation of lipoprotein lipase (choice A) appears to be the mechanism for lowering elevated VLDL levels by the fibric acids such as gemfibrozil. Bile acid- binding resins such as cholestyramine promote increased fecal excretion of bile acids (choice B) and ultimately lead to increased expression of hepatic LDL receptors.

QUESTION 575
Additive and potentially dangerous sedative interactions may occur between sedativehypnotic drugs and which of the following herbal preparations?

A. Echinacea
B. gingko biloba
C. ginseng
D. kava
E. St John's wort

Correct Answer: D
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Unregulated herbal preparations are in heavy use by the public and several have been documented to interact with regularly prescribed drugs. Kava (choice D) has sedative actions and interacts additively with sedativehypnotics and sedative-antihistaminics. Echinacea (choice A) has no reported drug interactions to date but many preparations contain alcohol, which may increase sedation with alcohol- containing beverages. Gingko biloba (choice B) has antiplatelet activity and should not be used with aspirin or other antiplatelet drugs. Ginseng (choice C) may cause CNS stimulation and should not be used by patients with epilepsy and those taking psychoactive drugs. St John's wort (choice E) may inhibit metabolism of certain drugs.

QUESTION 576
Figure shows plasma concentrations of drug W in a patient following intravenous (IV) injection of a single dose of 10 mg of the drug, an agent eliminated from the body by renal excretion. At hour 12, the patient is treated with sodium bicarbonate (arrow).

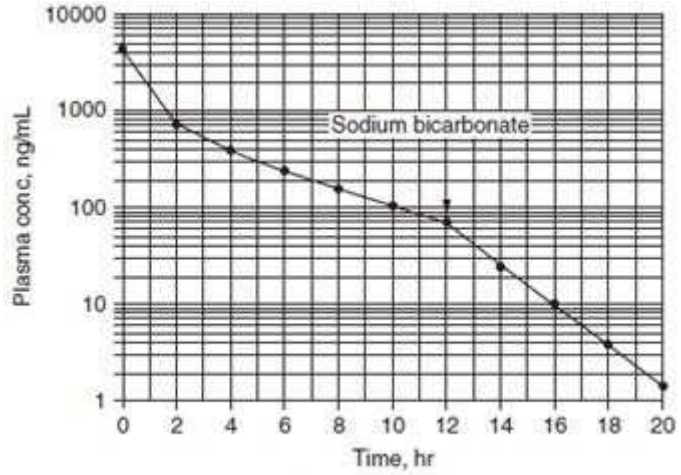


FIG. 6-1

Use the data before hour 12 to calculate the volume of distribution (Vd) for drug W.

A. 1 L
B. 10 L
C. 25 L
D. 50 L

E. 100 L

Correct Answer: B
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
The apparent volume of distribution is calculated using the equation = X/C, where is the

V_d

volume of distribution, X is the amount of drug present in the body, and C is the plasma (or blood) concentration. We must use time 0 for our calculations because this is the only time at which we know the amount of drug in the body; after administration it is immediately subjected to elimination. The curvature seen in the early data points results from distribution of the drug from blood into tissue compartments. The linear portion of the data reflects the elimination process and must be extrapolated back to time 0 to determine the plasma concentration that would have been obtained if distribution had been instantaneous. The administered dose of 10 mg divided by the extrapolated plasma concentration of 1000 ng/mL (1 mg/L) yields an apparent of 10 L. Volume of distribution is a useful parameter

V_d

that describes the relationship between the administered dose and the resulting plasma concentration. It is used for calculating loading doses.

QUESTION 577
Figure shows plasma concentrations of drug W in a patient following intravenous (IV) injection of a single dose of 10 mg of the drug, an agent eliminated from the body by renal excretion. At hour 12, the patient is treated with sodium bicarbonate (arrow).

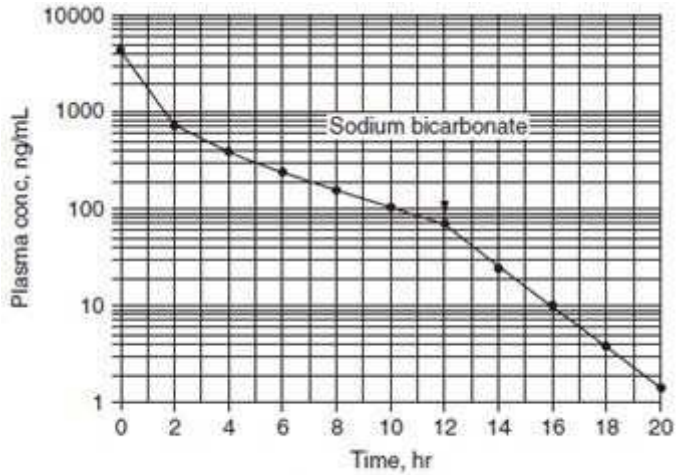


FIG. 6-1

Use the data before hour 12 to calculate the half-life ( ) for drug W.

$t_{\frac{1}{2}}$

A. 0.5 hour
B. 1 hour
C. 3 hours
D. 7 hours
E. 10 hours

Correct Answer: C
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
The apparent volume of distribution is calculated using the equation = X/C, where is the

V_d

volume of distribution, X is the amount of drug present in the body, and C is the plasma (or blood) concentration. We must use time 0 for our calculations because

this is the only time at which we know the amount of drug in the body; after administration it is immediately subjected to elimination. The curvature seen in the early data points results from distribution of the drug from blood into tissue compartments. The linear portion of the data reflects the elimination process and must be extrapolated back to time 0 to determine the plasma concentration that would have been obtained if distribution had been instantaneous. The administered dose of 10 mg divided by the extrapolated plasma concentration of 1000 ng/mL (1 mg/L) yields an apparent of 10 L. Volume of distribution is a useful parameter

V_d

that describes the relationship between the administered dose and the resulting plasma concentration. It is used for calculating loading doses.

QUESTION 578
The change in elimination rate after hour 12 when sodium bicarbonate was administered is expected if drug W is which of the following chemical types?

A. nonelectrolyte
B. strong acid
C. strong base
D. weak acid
E. weak base

Correct Answer: D
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
By inspection of the graph, it is observed that administration of sodium bicarbonate increases the rate of elimination of the drug (the slope of the line increases and the half-life is shortened). Sodium bicarbonate causes alkalinization of the urine. Alkalinization causes increased ionization of weak acids and accelerates their urinary excretion because the ionized (charged) forms cannot be easily reabsorbed through the tubular epithelium, whereas the uncharged forms of many weak acids are readily reabsorbed. Urinary alkalinization is a strategy sometimes used to hasten the excretion of weak acids, such as aspirin, in overdose situations. Excretion of a nonelectrolyte (choice A) is unaffected by changes in urinary pH because the polarity of nonelectrolytes is insensitive to pH. A strong acid (choice B) is fully ionized (unprotonated) at all attainable urinary pH values so that alteration of urinary pH has no effect on its excretion. A strong base (choice C) is similarly fully charged at all attainable urinary pH values so that alteration of urinary pH has no effect on its excretion. Excretion of a weak base (choice E) is slowed by alkalinization of urinary pH because the uncharged form of a base is readily reabsorbed from the tubular urine predominates.

QUESTION 579
Apatient calls 911 because of severe substernal crushing pain that has not responded to three nitroglycerin tablets taken sublingually. The paramedic team suspects that the patient has suffered an acute myocardial infarction. His blood pressure is 110/70 and his heart rate is 70, with occasional premature extra beats. What drug should be administered immediately, even before the patient reaches the hospital?

A. aspirin
B. dobutamine

C. lidocaine
D. metoprolol
E. streptokinase

Correct Answer: A
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Immediate administration of one aspirin tablet by mouth (choice A) has been shown to reduce morbidity and mortality from myocardial infarction. Because this dose is essentially free from adverse effects, this therapy is appropriate even before the diagnosis is confirmed by ECG or other means. Dobutamine (choice B) is a beta-1-selective agonist that has positive inotropic action. It is not appropriate at this time because there is no evidence of heart failure. Lidocaine (choice C), an antiarrhythmic, is not appropriate at this time because the patient is in sinus rhythm with only occasional arrhythmic beats. Metoprolol (choice D), a betablocking drug, is often used after the acute period of a myocardial infarction, but is inappropriate until the patient's condition is stabilized. Streptokinase (choice E), a thrombolytic agent, is inappropriate because coronary thrombosis has not been confirmed and this IV drug is given in the hospital setting.

QUESTION 580
Apatient calls 911 because of severe substernal crushing pain that has not responded to three nitroglycerin tablets taken sublingually. The paramedic team suspects that the patient has suffered an acute myocardial infarction. His blood pressure is 110/70 and his heart rate is 70, with occasional premature extra beats. After initial treatment in the hospital, the patient. is found to be suffering from more severe hypotension (his blood pressure is now 70/40) and reduction of cardiac function with reduced left ventricular ejection fraction. His urine output is low and he has mental clouding. Which of the following is the pharmacologic treatment of choice for this condition in this patient?

A. atenolol
B. digoxin
C. dopamine
D. norepinephrine
E. procainamide

Correct Answer: C
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
The description of the patient's reduced cardiac function and elevated left ventricular filling pressure, with reduced peripheral perfusion (clouded mentation, reduced urine output) indicates cardiogenic shock, decreased blood pressure due to decreased cardiac output. In cardiogenic shock, a drug is needed that increases myocardial contractility without increasing heart rate and peripheral resistance. In addition, renal artery dilation is desirable to prevent renal shutdown. Dopamine (choice C), an agonist at dopamine, beta-, and alphaadrenoceptors, increases myocardial contractility with little increase in peripheral resistance and

lower renal arterial resistance. Atenolol (choice A), a beta-1-selective blocker, is inappropriate in the setting of reduced cardiac function, although it may be quite appropriate later when the patient's condition is stabilized. Digoxin (choice B), a cardiac glycoside, may increase cardiac contractility but has a slow onset of action and may exacerbate arrhythmias. Norepinephrine (choice D) increases myocardial contractility but also greatly increases peripheral resistance, a situation that must be avoided in cardiogenic shock. Procainamide (choice E), a group IA antiarrhythmic agent, is not indicated because the patient does not have an arrhythmia.

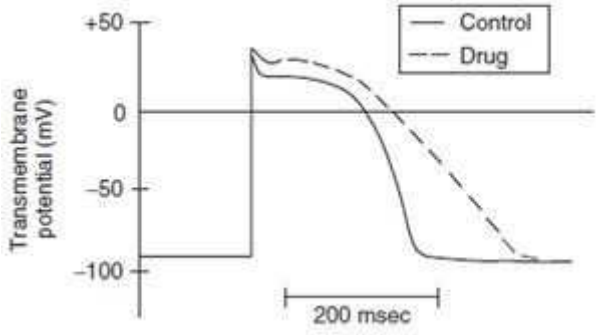
QUESTION 581
Apatient is being treated for metastatic prostate cancer. Which of the following agents is used parenterally in prostate cancer to reduce luteinizing hormone (LH) release from the pituitary even though it initially increases LH release?

A. diethylstilbestrol
B. finasteride
C. flutamide
D. ketoconazole
E. leuprolide

Correct Answer: E
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Leuprolide is a GnRH agonist that when given in pulsatile fashion stimulates pituitary LH release, but when given continuously, or in a depot preparation, suppresses LH release and reduces plasma testosterone levels to castration levels. Because it is a peptide, it must be given parenterally. It is used extensively in the treatment of metastatic prostate cancer. Diethylstilbestrol (choice A) is an oral nonsteroidal synthetic estrogen that is now rarely used in the treatment of prostate cancer. Use of this agent produces undesirable feminization and is reserved for cases unresponsive to other agents. Finasteride (choice B) is an orally active inhibitor of the 5-alpha-reductase that converts testosterone to dihydrotestosterone in the prostate. Because conversion of testosterone to dihydrotestosterone is essential for the androgenic effects in the prostate, inhibition of the 5-alpha-reductase decreases the stimulation of the prostate. Unfortunately, the drug has limited efficacy in prostate malignancy. Finasteride is used for the treatment of benign prostatic hyperplasia because it produces a moderate decrease in prostate size and improvement in urinary flow. It is also used for the treatment of androgenic hair loss. Flutamide (choice C) is a nonsteroidal antiandrogen occasionally used in the treatment of prostate cancer that is unresponsive to leuprolide. It is active orally. Ketoconazole (choice D) is an oral antifungal agent that has the property of inhibiting the cytochrome P450 isoforms involved in steroid biosynthesis. It has been used in the treatment of prostate cancer with mixed results.

QUESTION 582
A drug being developed as an antiarrhythmic agent was studied in the laboratory using microelectrode techniques for measuring the transmembrane potential. The results of this study are shown in below figure. Which of the following standard antiarrhythmic agents does the new drug most resemble?



A. adenosine
B. ibutilide
C. lidocaine
D. procainamide
E. propranolol

Correct Answer: B
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
The recorded transmembrane potential indicates that the new drug has no effect on the upstroke velocity but prolongs the action potential duration of the ventricular muscle fiber. This effect is characteristic of blocking potassium ( ) channels that open during repolarization, actions shown by

I_k

group III antiarrhythmic drugs such as ibutilide. Adenosine (choice A) hyperpolarizes AV nodal cells and blocks propagation of impulses through this part of the heart. It does not prolong the action potential. Lidocaine (choice C) is a group IB drug and slows upstroke velocity of the action potential in susceptible cells but shortens, rather than prolongs, the action potential duration. Procainamide (choice D) is a group IA drug that slows upstroke velocity as well as prolonging the action potential. Propranolol (choice E), a beta blocker, is a group II drug and has little effect on ventricular cell action potentials at clinically relevant concentrations.

QUESTION 583
A patient is admitted for acute coronary syndrome with signs of impending myocardial infarction. She undergoes angioplasty with double coronary stenting to maintain the patency of her coronary vessels. Which of the following drugs will probably be administered to prevent clotting in the region of the wire mesh stents?

A. clopidogrel

B. low-molecular-weight heparin
C. regular heparin
D. tissue plasminogen activator (t-PA)
E. warfarin

Correct Answer: A
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Foreign material (such as a stent) in blood vessels invites clotting and the stented vessel will rapidly occlude if clotting is not prevented. The primary process in the formation of this arterial clot is platelet aggregation, so an antiplatelet drug such as clopidogrel is suitable (choice A). Abciximab and tirofiban are also sometimes used in this setting. Heparin (both forms, choices B and C) and warfarin (choice E) are useful in the prevention of venous thrombosis. t-PA (choice D) is useful in accelerating the dissolution of a fibrin clot (e.g., after myocardial infarction), but is not useful in this situation.

QUESTION 584
Which of the following acts as a folate antagonist in the treatment of malaria?

A. amodiaquine
B. chloroquine
C. mefloquine
D. proguanil
E. quinine

Correct Answer: D
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Proguanil is a prodrug that is converted to cycloguanil, an inhibitor of malarial dihydrofolate reductase. Amodiaquine (choice A) and chloroquine (choice C) are similar and probably interfere with metabolism of heme in the vacuoles of the parasite. Mefloquine (choice C) and quinine (choice E) have unknown mechanisms of action but are not folate antagonists.

QUESTION 585
Which of the following antiviral drugs is correctly associated with the appropriate primary toxicity?

A. amantadine--neutropenia

B. didanosine--pancreatitis
C. ribavirin--hepatitis
D. ritonavir--hemolytic anemia
E. zidovudine--CNS stimulation, GI complaints

Correct Answer: B
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Didanosine causes pancreatitis in a significant number of patients treated for AIDS. Amantadine (choice A) is used in the prevention and treatment of influenza and causes CNS stimulation and light headedness. Ribavirin (choice C) is used for the treatment of respiratory syncytial virus in infants and causes dose-dependent hemolytic anemia in about 10% of patients. Ritonavir (choice D), a protease inhibitor used in AIDS, causes hepatitis. Zidovudine (choice E), another drug used in AIDS, causes neutropenia as its primary doselimiting effect.

QUESTION 586
Which of the following antiviral agents uses viral thymidine kinase as part of its activation pathway?

A. acyclovir
B. amantadine
C. foscarnet
D. saquinavir
E. zidovudine

Correct Answer: A
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Acyclovir is an acyclic guanine nucleoside analog that undergoes activation by phosphorylation by herpesviral thymidine kinase (but not the host thymidine kinase) to form the acyclovir triphosphate form and causes DNA chain termination. Amantadine (choice B) is a tricyclic amine that inhibits uncoating of influenza A virus. It is also used for the treatment of parkinsonism. Foscarnet (choice C) is a pyrophosphate analog that inhibits herpesvirus nucleic acid synthesis at the level of the viral DNA polymerase. Saquinavir (choice D) is an HIV protease inhibitor. Zidovudine (choice E) is an antiretroviral thymidine analog. The triphosphate is a competitive inhibitor of reverse transcriptase and a DNA chain terminator. The monophosphate is a competitive inhibitor of thymidine kinase.

QUESTION 587
Resistance to which of the following drugs occurs when the bacterium expresses higher quantities of a drug-efflux pump?

A. amoxicillin
B. clarithromycin
C. doxycycline
D. gentamicin
E. vancomycin

Correct Answer: C
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Resistance to tetracyclines such as doxycycline (choice C) is associated with production of an efflux pump or alteration of the 30S ribosomal-binding site. Resistance to beta lactams such as amoxicillin (choice A) usually results from production of beta lactamase. Macrolides such as clarithromycin (choice B), erythromycin, and azithromycin bind to the 50S ribosome in susceptible organisms and prevent protein synthesis. Simple methylation of the binding site prevents the bacteriostatic action of these drugs and many bacteria have such mutation. Resistance to aminoglycosides such as gentamicin (choice D) is usually due to synthesis of inactivating enzymes by the bacteria. Resistance to vancomycin (choice E) is still unusual but can occur through the modification of the D-ala-D-ala-binding site in peptidoglycan.

QUESTION 588
Which of the following antitubercular agents is a strong inducer of hepatic cytochrome P450?

A. ethambutol
B. isoniazid
C. rifampin
D. streptomycin
E. sulfisoxazole

Correct Answer: C
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Rifampin selectively inhibits bacterial DNA-dependent RNA polymerase. It is very useful in treating mycobacterial infections since it can penetrate cells and kill intracellular organisms. It is one of the most potent inducers of cytochrome P450 known, leading to increased hepatic clearance of many other drugs including the oral anticoagulants, cyclosporine, propranolol, digitoxin, corticosteroids, and oral contraceptives. Ethambutol (choice A) is often combined with isoniazid in antitubercular regimens. Clearance is primarily via renal excretion. Isoniazid (choice B) is the most widely used antitubercular agent. It functions by inhibiting

mycolic acid biosynthesis. Isoniazid is cleared by metabolism via N- acetylase and hydrolytic activity. Streptomycin (choice D) was the first effective drug for the treatment of tuberculosis, but, because of its ototoxicity and nephrotoxicity and the development of less toxic agents, use of streptomycin is limited to more severe forms of the disease. Sulfisoxazole (choice E) may rarely be used in antitubercular regimens in combination with other drugs. Clearance is primarily via glomerular filtration.

QUESTION 589
A 35-year-old woman with hypertension is planning to become pregnant. Which of the following is contraindicated in pregnancy?

A. clonidine
B. hydralazine
C. hydrochlorothiazide
D. losartan
E. methyldopa

Correct Answer: D
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Losartan causes renal damage in the fetus, and renal impairment in renovascular disease. It is contraindicated in pregnancy. Clonidine (choice A) causes some sedation and rebound hypertension when stopped suddenly, but is not contraindicated in pregnancy. Hydralazine (choice B) causes a reversible type of lupus erythematosus. Hydrochlorothiazide (choice C) may cause hypokalemia, dilutional hyponatremia, elevated lipids, hyperuricemia, and glucose intolerance. Methyldopa (choice E) causes sedation and formation of red blood cell antibodies, but has been shown to be safe in pregnancy.

QUESTION 590
A 35-year-old opera singer has been treated for hypertension with enalapril. Although his blood pressure has been reduced, he complains that he is now unable to perform because of a dry cough. Which of the following acts by a similar but not identical mechanism and is much less likely to cause cough?

A. captopril
B. clonidine
C. losartan
D. prazosin
E. propranolol

Correct Answer: C
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Losartan, an A receptor-blocking agent, has effects in hypertension similar to those of ACE

T_1

inhibitors but causes a much lower incidence of cough. Captopril (choice A) and other ACE inhibitors cause a dry cough in 520% of patients. This may be due to accumulation of bradykinin as a result of ACE inhibition; ACE also metabolizes bradykinin. The cough disappears with cessation of ACE inhibitor treatment. Pretreatment with aspirin reduces its frequency and severity in some patients. Clonidine (choice B), the centrally acting alpha- 2-receptor agonist, produces sedation and xerostomia but not cough. The alpha-1-receptor antagonist prazosin (choice D) produces postural hypotension but not cough. The betablocker propranolol (choice E) may produce a variety of side effects including precipitating heart failure and asthma in susceptible patients. It does not cause cough. Propranolol has been used by musicians to control palpitations associated with stage fright.

QUESTION 591
Which of the following agents used in treating testicular cancer, requires hydration and dieresis to prevent renal toxicity?

A. bleomycin
B. cisplatin
C. cyclophosphamide
D. 5-fluorouracil
E. paclitaxel

Correct Answer: B
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Cisplatin binds to DNA where it forms intra- and interstrand crosslinks. Cisplatin is particularly effective in testicular and ovarian cancers in combination with other antitumor agents. Cisplatin exerts a renal toxicity that may be prevented by the infusion of saline to maintain a high urine flow. Ototoxicity involving high-frequency hearing loss is an effect that is not prevented by hydration. The natural product bleomycin (choice A) binds to DNA and causes single- and double-strand breaks, leading to cytotoxicity. The drug is particularly useful against Hodgkin lymphoma and testicular tumors. Bleomycin has the serious toxicity of pulmonary fibrosis. Cyclophosphamide (choice C) is widely used in combination regimens. Nausea and vomiting are the most common toxicities. Hemorrhagic cystitis may be minimized by hydration and use of the drug mesna. Note that this toxicity is not at the level of the kidney. The pyrimidine analog 5-fluorouracil (5-FU) (choice D) is used to treat a wide variety of carcinomas. Toxicity from 5-FU is expressed as GI disturbances (anorexia, nausea, stomatitis, and diarrhea) and myelosuppression. Paclitaxel (choice E) is particularly useful in treating metastatic breast and ovarian cancer. The primary toxicity of paclitaxel is bone marrow suppression.

QUESTION 592
Which of the following chemotherapeutic agents' mechanisms of action involve inhibition of thymidylate synthase and incorporation into RNA?

A. anastrozole
B. cytarabine
C. doxorubicin
D. 5-fluorouracil
E. imatinib

Correct Answer: D
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
The pyrimidine analog 5-fluorouracil (5-FU) is metabolized by ribosylation and phosphorylation to the nucleotide level (F-UMP). F-UMP is further metabolized to F-dUMP, an inhibitor of thymidylate synthase. Cells then become starved for TTP and incorporate FdUTP and dUTP in its place in DNA. 5- FU also becomes incorporated in RNA, leading to inhibition of RNAprocessing. Anastrozole (choice A) is a nonsteroidal inhibitor of aromatase, an enzyme required for synthesis of estrogens. This drug is useful against advanced estrogen or progesterone receptor-positive breast cancer. Cytarabine (cytosine arabinoside, ara-C, choice B), is an S-phase-specific antimetabolite that is metabolized to the triphosphate form, which blocks DNA synthesis. It is used exclusively in acute myelogenous leukemia. Doxorubicin (choice C) is an anthracycline antibiotic that intercalates into DNA causing strand breakage and blockage of both DNA and RNA synthesis. This agent is widely used in combination regimens for breast, endometrial, ovarian, testicular, and thyroid carcinomas, and several sarcomas and lymphomas. Imatinib (choice E) is an inhibitor of the tyrosine kinase activity of the Bcr-Abl oncogene product. It is a drug of choice in chronic myelogenous leukemia with the Philadelphia chromosome translocation.

QUESTION 593
Which of the following chemotherapeutic agents' mechanisms of action involves inhibition of topoisomerase II and results in DNA strand breakage?

A. dacarbazine
B. etoposide
C. lomustine
D. prednisone
E. vincristine

Correct Answer: B
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Etoposide is a semisynthetic derivative of podophyllotoxin, a constituent of the mandrake plant. Etoposide is an inhibitor of topoisomerase II, an enzyme that relaxes supercoiled DNA by breaking one strand and passing the second strand through the break before closing the break. Etoposide inhibits the closure step and

results in an accumulation of DNA strand breaks, leading to cell death. Etoposide is used to treat testicular tumors and small cell carcinoma of the lung in combination with cisplatin. Leukopenia is the dose-limiting toxicity seen with this drug. Dacarbazine (choice A) is a synthetic prodrug activated in the liver to a metabolite that alkylates DNA leading to cytotoxicity. The drug is useful against melanoma and Hodgkin lymphoma. Lomustine (CCNU, choice C) is a lipid-soluble nitrosourea agent that acts as an alkylating agent. The nitrosoureas are unusual in having relatively good access to the CNS and are therefore useful in treating brain tumors. Prednisone (choice D) is a potent, orally active corticosteroid with good lymphotoxic potency. Its mechanism is not fully understood but may involve activation of apoptotic pathways in lymphocytes. Vincristine (choice E) is a natural product isolated from the vinca plant. It is classified as a spindle poison and inhibits mitosis by inhibiting microtubule assembly. This drug is particularly useful in treating acute leukemias in children and Hodgkin lymphoma.

QUESTION 594
A 13-year-old boy with severe asthma has been treated for 6 months with good control of nocturnal wheezing. His parents now complain that he seems to be very fat around the face and shoulders, bruises easily, and has discolored streaks on his abdomen. Laboratory tests reveal moderate hyperglycemia. He has probably been receiving which of the following drugs?

A. ipratropium
B. prednisone
C. salmeterol
D. terbutaline
E. theophylline

Correct Answer: B
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
This patient's presentation is typical of glucocorticosteroid toxicity (iatrogenic Cushing syndrome). Prednisone is an effective corticosteroid frequently used by mouth to control severe asthma that is not responsive to inhaled corticosteroids. High doses of prednisone, given chronically, very predictably cause signs and symptoms of hypercorticism. Ipratropium (choice A) is an antimuscarinic agent used in asthma by inhalation. Salmeterol (choice C) is a long-acting beta-2-selective agonist used by inhalation. Terbutaline (choice D) is a shortacting beta-2-selective agonist, also used by inhalation. Theophylline (choice E) is an oral drug that causes CNS stimulation (including convulsions in toxic overdosage), but not hypercorticism.

QUESTION 595
Which of the following describes a possible adverse effect of long-term chronic treatment of schizophrenia with a phenothiazine such as fluphenazine?

A. diarrhea, nausea, and vomiting
B. reduced secretion of prolactin
C. tardive dyskinesia
D. Tourette syndrome
E. weight loss

Correct Answer: C
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Long-term treatment of schizophrenia with potent dopamine receptor antagonists is associated with

D_2

a high incidence of the irreversible extrapyramidal dystonias called tardive dyskinesia. The phenothiazines (and haloperidol) are receptor antagonists in the CNS; their success in the treatment

D_2

of schizophrenia resulted in the hypothesis that the antipsychotic effect requires blockade. Data

D_2

from newer, atypical antipsychotic agents casts some doubt on this hypothesis because drugs, such as clozapine and risperidone, have a low affinity for receptors. Older drugs in the phenothiazine class

D_2

(e.g., chlorpromazine) have both antimuscarinic and antiemetic action; thus diarrhea, nausea, and vomiting (choice A) are very unlikely. Because prolactin secretion (choice B) from the anterior pituitary is inhibited by dopamine, blockade of receptors by fluphenazine increases prolactin

D_2

secretion. This may result in breast engorgement and galactorrhea in women. Tourette syndrome (choice D) involves tics and other involuntary movements and obscene vocalizations. The neuroleptic agent haloperidol is the current drug of choice for the treatment of this disease. Weight loss (choice E) is associated with the use of selective SSRIs, not phenothiazines. In fact, the phenothiazines are often associated with weight gain.

QUESTION 596
Which of the following psychotropic drugs must be monitored for hematotoxic effects?

A. buspirone
B. clozapine

C. haloperidol
D. lithium carbonate
E. mirtazapine

Correct Answer: B
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Clozapine causes agranulocytosis in a small but consistent fraction of patients; monitoring is mandatory. Buspirone (choice A) is an antianxiety agent with minimal sedative action. Haloperidol (choice C) is an older, highly potent antipsychotic drug used in schizophrenia. Lithium carbonate (choice D) is an important antimanic drug. It apparently acts by interfering with inositol phosphate cycling and second messenger synthesis in neurons. Mirtazapine (choice E) is a third-generation antidepressant related to antihistaminics and has significant sedative action.

QUESTION 597
Which of the following is used in treating major depression and has the greatest sedative effect?

A. bupropion
B. desipramine
C. fluoxetine
D. mirtazapine
E. venlafaxine

Correct Answer: D
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
All of the agents listed are useful antidepressants but only mirtazapine has significant sedative effects.

QUESTION 598
Which of the following is the drug of choice to reverse bronchoconstriction in an acute asthma attack?

A. albuterol
B. aminophylline
C. cromolyn
D. ipratropium

E. salmeterol

Correct Answer: A
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Inhaled albuterol (or other beta-2-selective receptor agonists including bitolterol, metaproterenol, pirbuterol, and terbutaline) are the usual agents of choice for treating bronchoconstriction in an acute asthma attack. These beta-2-selective agonists produce bronchial relaxation by stimulating cyclic AMP (cAMP) formation in bronchiolar smooth muscle and cause less tachycardia than nonselective beta agonists. Unfortunately, they do cause some tachycardia and skeletal muscle tremor. Aminophylline (choice B) and other methylxanthines are rarely used to terminate acute episodes of asthma because they must be administered parenterally for rapid onset of effect. Cromolyn sodium (choice C) must be used prophylactically to prevent acute episodes and probably acts by stabilizing mast cells. It is not a smooth muscle relaxing agent and is not effective in reversing bronchospasm. Inhaled ipratropium (choice D) has less general efficacy in acute attacks than beta agonists. Salmeterol (choice E) is an effective beta-2-selective agonist but has a slow onset and long duration of action. Therefore, it is used for prophylaxis, not treatment of acute attacks.

QUESTION 599
Which of the following drugs is useful in treatment of gout with recurrent renal urate stones because it decreases the excretion of uric acid?

A. allopurinol
B. aspirin
C. colchicines
D. indomethacin
E. sulfinpyrazone

Correct Answer: A
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Allopurinol and its metabolite alloxanthine inhibit xanthine oxidase, thus preventing conversion of xanthine and hypoxanthine to uric acid. Although xanthine and hypoxanthine then accumulate, these compounds are more soluble than uric acid and less likely to deposit in joints or precipitate in the urine. Most doses of aspirin (choice B) increase retention of uric acid, especially low doses. Colchicine (choice C) is an inhibitor of microtubule function that brings relief in an acute gout attack by inhibiting the motility of granulocytes and preventing the formation of mediators of inflammation by leukocytes. Because of its toxicity at higher doses, it is now used chiefly at low doses to prevent acute attacks. Indomethacin (choice D) is an NSAID that inhibits COX and reduces formation of prostaglandins and eicosanoids involved in gouty arthritis. It has no effect on the formation of uric acid and very little on its excretion. Sulfinpyrazone (choice E) and probenecid are uricosuric agents--they increase the excretion of uric acid by the kidney. Renal uric acid excretion is determined by the balance between the amount filtered plus that actively secreted and the amount undergoing passive and active reabsorption. At very low doses, these agents inhibit active secretion and thus promote

retention of uric acid. At higher (clinical) doses, both active secretion and active reabsorption are inhibited, with the result that excretion is enhanced.

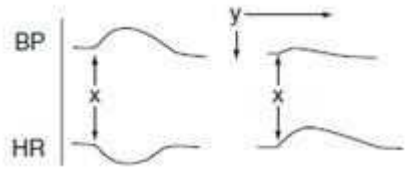
QUESTION 600
Which of the following drugs can be used in rheumatoid arthritis with the lowest probable incidence of GI complications?

A. aspirin
B. celecoxib
C. ibuprofen
D. misoprostol
E. naproxen

Correct Answer: B
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
A through C and E are NSAIDs. NSAIDs have long been drugs of first choice in arthritis treatment. Their primary mechanism of action in arthritis appears to be inhibition of COX, an enzyme required for the synthesis of inflammatory and other prostaglandins. Two forms of COX are present in the body:
COX-1, which is required for synthesis of several useful prostaglandins (e.g., PGE1, a cytoprotective agent in the stomach), and COX-2, the isoform responsible for synthesis of prostacyclin as well as most of the damaging prostaglandins. Celecoxib is more selective for COX-2 and thus has a lower incidence of adverse GI effects. The older NSAIDs (choices A, C, and E) inhibit both COX-1 and COX-2 with less selectivity and thus reduce protective prostaglandins, resulting in a high incidence of GI disorders, especially peptic ulceration. Misoprostol (choice D) is a PGE1 analog that is used with NSAIDs to reduce peptic ulceration; unfortunately it causes a high incidence of diarrhea.

QUESTION 601
In a study of cardiovascular drugs, normal volunteers were given drug X in a small bolus dose while blood pressure and heart rate were recorded. After recovery, a long-acting blocking agent, Y, was administered. The direct effects of Y were not recorded. After drug Y had equilibrated with the tissues of the body, drug X was repeated in the same dosage. The results are shown in below figure.



Drug X behaves most like which of the following?

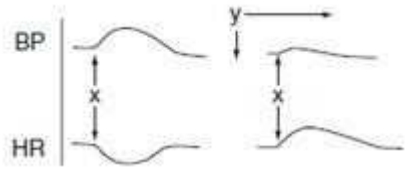
A. bethanechol

B. epinephrine
C. isoproterenol
D. norepinephrine
E. phenylephrine

Correct Answer: D
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Elevated blood pressure typically evokes a compensatory baroreceptor reflex with slowing of heart rate. Thus, the decrease in heart rate shown in the initial data can be interpreted as a reflex bradycardia. Bethanechol (choice A) is a muscarinic agonist and typically causes vasodilation, with a drop in blood pressure and a compensatory tachycardia. Epinephrine (choice B), an alpha-1-, alpha-2-, beta-1-, and beta-2-agonist, causes hypertension at high doses, but usually also causes tachycardia. Isoproterenol (choice C) is a beta-1-, beta-2- agonist, and does not cause hypertension or bradycardia. Norepinephrine (choice D) and phenylephrine (choice E) can both cause hypertension and reflex bradycardia. However, norepinephrine has beta-1-agonist action, whereas phenylephrine has only alpha effects. Thus, in the presence of an alpha-blocking agent, norepinephrine causes a beta-1-mediated tachycardia; phenylephrine has no effect on heart rate.

QUESTION 602
In a study of cardiovascular drugs, normal volunteers were given drug X in a small bolus dose while blood pressure and heart rate were recorded. After recovery, a long-acting blocking agent, Y, was administered. The direct effects of Y were not recorded. After drug Y had equilibrated with the tissues of the body, drug X was repeated in the same dosage. The results are shown in below figure.



Drug Y behaves most like which of the following?

A. atropine
B. pralidoxime
C. prazosin
D. reserpine
E. timolol

Correct Answer: C

Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
As noted in the answer to question 75, the agonist drug in the data presented is th~e alpha and beta-1 agonist norepinephrine. Prazosin (choice C) is an alpha blocker that prevents the pressor effects of alpha agonists such as norepinephrine and phenylephrine. If norepinephrine's alpha-agonist effects on the vessels are blocked, its beta-agonist action on the heart becomes evident, causing tachycardia. Phenylephrine, on the other hand, has no betaagonist effects, and tachycardia does not result. Atropine (choice A) is a muscarinic blocker and does not prevent hypertension due to alpha agonists. Pralidoxime (choice B) is a cholinesterase regenerator used in the treatment of organophosphate insecticide toxicity. Reserpine (choice D) is a blocker of postganglionic sympathetic nerve function (it prevents storage of norepinephrine in transmitter vesicles and depletes the nerve ending of its transmitter stores); it has no effect in the experiment described. Timolol (choice E), a beta blocker, does not prevent the pressor effects of alpha agonists.

QUESTION 603
Which of the following conditions is a primary indication for the use of esmolol?

A. arrhythmia associated with thyroid storm
B. chronic heart failure
C. chronic hypertension
D. diabetic nephropathy
E. familial tremor

Correct Answer: A
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Esmolol is a very short-acting, parenteralonly beta-blocking drug. Transient arrhythmias such as those occurring during thyrotoxicosis are frequently responsive to the drug. Because the drug must be given parenterally and has duration of action of only 15 minutes, it is unsuited for any chronic condition (choices BE).

QUESTION 604
Which of the following agents would cause the greatest increase in heart rate in a functioning transplanted heart?

A. amphetamine
B. cocaine
C. ephedrine
D. isoproterenol
E. terbutaline

Correct Answer: D
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
The transplanted heart lacks functional innervation for at least 2 years after surgery, and possibly longer. Because the nerves are cut in the procedure, nerve endings degenerate (Wallerian degeneration) and transmitter stores are lost. Adrenoreceptors on the denervated myocardial cells are normal or even increased in sensitivity, so responses to direct-acting betaadrenoreceptor agonists such as isoproterenol are retained. Indirectly acting sympathomimetics, on the other hand, are relatively ineffective (choices A, B, and C) because they act through the release or amplification of endogenous

QUESTION 605
Which of the following agents produces vasodilation by increasing nitric oxide synthesis in endothelial cells?

A. diazoxide
B. histamine
C. minoxidil
D. nitroprusside
E. verapamil

Correct Answer: B
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Histamine activates nitric oxide synthase by binding to receptors in the endothelium. Nitric oxide

H_1

synthesis is increased, and this molecule rapidly diffuses into the adjoining smooth muscle, where it causes vasodilation. Diazoxide (choice A) is a powerful vasodilator used in hypertensive emergencies. It acts by opening potassium channels in vascular smooth muscle and hyperpolarizing these cells. Minoxidil (choice C), another vasodilator used in severe hypertension, is converted to the sulfate metabolite, which similarly opens potassium channels and hyperpolarizes vascular smooth muscle. Nitroprusside (choice D) contains nitric oxide that is spontaneously released in the blood. Stimulation of endothelial synthesis is not involved. Verapamil (choice E) blocks calcium channels in vascular smooth muscle and thereby causes relaxation.

QUESTION 606
Which of the following statements correctly associates a CNS drug with its mechanism of action?

A. bupropion--activation of endocannabinoid receptors
B. diazepam--facilitation of GABAstimulated chloride channel opening
C. fluoxetine--selective inhibition of presynaptic norepinephrine reuptake
D. pentobarbital--inhibition of NMDA receptors
E. tranylcypromine--inhibition of O-methylation of catecholamines

Correct Answer: B
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
The benzodiazepine agents, including diazepam, facilitate the actions of the inhibitory neurotransmitter GABA, which acts on GAB receptors to open chloride ion channels. Bupropion (choice A) is

probably an inhibitor of norepinephrine and dopamine uptake and does not act on GABA receptors. Fluoxetine (choice C) is a selective inhibitor of serotonin uptake. Pentobarbital (choice D) is a modulator of the same GABA-sensitive chloride channel affected by benzodiazepines, although its mechanism of action is slightly different. Tranylcypromine (choice E) is an inhibitor of MAO rather than catechol-O-methyltransferase (COMT).

QUESTION 607
Which of the following agents is associated with numerous drug-drug interactions because of its inhibition of hepatic cytochrome P450 activity?

A. atracurium
B. cromolyn
C. ketoconazole
D. Phenobarbital
E. rifampin

Correct Answer: C
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Ketoconazole is a potent inhibitor of cytochrome P450 isozymes; its antifungal action is the result of inhibition of fungal P450. Atracurium (choice A) is used to produce skeletal muscle relaxation during surgery. Atracurium is eliminated by a spontaneous chemical reaction and by plasma cholinesterases, and is not a substrate or inhibitor of cytochrome P450. Cromolyn sodium (choice B) is not a substrate or inhibitor of cytochrome P450. The extremely small amounts of this drug

that are absorbed are excreted unchanged in the urine and bile. Phenobarbital (choice D) is eliminated by cytochrome P450 metabolism, and is an inducer of drug metabolism activity. Rifampin (choice E) similarly produces many drug interactions because of its ability to induce (rather than inhibit) cytochrome P450 activity.

QUESTION 608
A patient has completed a course of cancer chemotherapy and now has severe anemia, neutropenia, and thrombocytopenia. If only one intervention is possible, which of the following is the most appropriate therapy?

A. epoetin (erythropoietin)
B. filgrastim (G-CSF)
C. growth hormone
D. sargramostim (GM-CSF)
E. testosterone

Correct Answer: D
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Apatient who is anemic, neutropenic, and thrombocytopenic requires stimulation of all three major cell lines in the bone marrow. The only drug currently available that accomplishes this broad-spectrum stimulant effect is sargramostim (granulocytemacrophage colony stimulating factor [GM-CSF]). Epoetin (choice A) is a more selective stimulant of erythrocyte production and is useful in simple anemia. Filgrastim (choice B) is a somewhat selective stimulant of leukocyte production and has much less effect on erythrocytes and platelet production than sargramostim. Growth hormone (choice C) and testosterone (choice E) have both been tried in the treatment of anemia with negligible success.

QUESTION 609
The most rapid onset of action of inhaled general anesthetics correlates with the smallest value for which of the following variables?

A. blood-gas partition coefficient
B. MAC
C. molecular size
D. oilwater partition coefficient
E. onset of hepatic metabolism

Correct Answer: A
Section: Pharmacology
Explanation

Explanation/Reference:

Explanation:
The blood-gas partition coefficient is a measure of the solubility of the inhalation anesthetic in the blood relative to its solubility in the inspired air. Circulating blood provides the means of anesthetic delivery to the brain and the partial pressure determines the rate of transfer into the CNS. The solubility of an agent in blood determines how rapidly the partial pressure rises in the blood. Agents with high solubility (large blood-gas partition coefficients) require large amounts of the anesthetic to dissolve in the blood before the partial pressure in the blood increases enough to effectively deliver them to the brain. Thus, agents with lower blood solubilities (small blood-gas partition coefficients) have more rapid rates of onset of anesthesia. Desirable properties for inhalation anesthetic agents include high potency and low blood solubility. The halogenated hydrocarbons, such as desflurane and sevoflurane, fit these criteria and are used extensively. The MAC value (median alveolar anesthetic concentration) required for anesthesia (choice B) is a measure of the potency of the agent, but does not give an indication of the rate of onset of anesthesia. Molecular size (choice C) may play a role in determining the blood-gas partition coefficient, but it is only a partial determinant. The oilwater partition coefficient (choice D) is a measure of the lipid solubility of the anesthetic agent. This correlates with the potency as measured by the MAC. Hepatic metabolism (choice E) plays no role in onset of action, but may be important in terms of possible liver and kidney damage resulting from the production of toxic metabolites from some of the halogenated inhaled anesthetic agents.

QUESTION 610
Which of the following inhaled general anesthetic agents has an MAC that exceeds normal atmospheric pressure?

A. enflurane
B. halothane
C. isoflurane
D. nitrous oxide
E. sevoflurane

Correct Answer: D
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
The MAC value for nitrous oxide is 105110 % (i.e., 510% greater than atmospheric pressure), meaning that for nitrous oxide to be used as the sole anesthetic agent, hyperbaric conditions would have to be used to deliver both the nitrous oxide for anesthesia and oxygen needed for life. The other commonly used inhaled agents, including the halogenated hydrocarbons enflurane, isoflurane, halothane, and sevoflurane (choices A, B, C, and E) have MAC values of 6% or less. Although these data might be interpreted to imply that nitrous oxide is not useful in anesthesia, nitrous oxide is very valuable because of its very low toxicity and additive effects with more potent (but more toxic) agents. It is therefore commonly combined with other inhaled agents, especially the halogenated hydrocarbons. For example, 0.5% MAC of nitrous oxide plus 0.5% MAC of isoflurane delivers a full anesthetic concentration of gases to the lungs but requires <60% of the inspired air partial pressure, so oxygen can utilize the other 40%.

QUESTION 611
Exhibit:

A. desiccated thyroid
B. levothyroxine (T_4)
C. liothyronine (T_3)
D. potassium iodide
E. reverse T_3

Please refer to the exhibit.
Which of the following is the agent of choice for chronic treatment of simple hypothyroidism (myxedema)?

A. A
B. B
C. C
D. D
E. E

Correct Answer: B
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
The agent of choice in treating simple hypothyroidism is levothyroxine ( ). Administered thyroxine

T_4

is bound in plasma in the same way and metabolized to tri-iodothyronine in the same manner as native thyroxine. Although liothyronine (tri-iodothyronine [ ] choice C) is more active than as an

T_3

agonist at thyroid hormone receptors, its shorter half-life of 1 day as compared with the 67-day half- life of means that thyroxine has a longer duration of action and provides smoother control. The use

T_4

of desiccated thyroid (choice A) has been abandoned in the United States because of variations in potency. T4 (3,5,3',5'-tetraiodothyronine) is converted by deiodinases to the active (3,5,3'-

T_3

triiodothyronine) and the inactive reverse (3,3',5'-triiodothyronine [choice E]) in equal amounts.

T_4

is used in therapy under special circumstances when immediate thyroid effect is required, but it is not generally used to treat hypothyroidism because of its higher cost and shorter duration of action. At high concentrations, iodide in the form of potassium (choice D) or other salts is an inhibitor of thyroid gland function and is used in hyperthyroidism. Iodide inhibits its own uptake into thyroid cells and inhibits the release of thyroxine and from the gland. Iodide treatment is useful in preparation for surgical

T_4

thyroidectomy because the gland becomes firmer and vascularity is reduced.

QUESTION 612
A 24-year-old woman presents with hypertension and hypokalemic metabolic alkalosis. Although these symptoms are normally indicative of hyperaldosteronism, this patient's aldosterone levels are undetectable, and no other mineralocorticoid activity is found. A diagnosis of Liddle syndrome is made on the basis of the signs and symptoms and a family history. Liddle syndrome is caused by a genetic defect leading to excessive expression of the apical sodium channel in the principal cells of the cortical- collecting tubule and excess sodium transport in this part of the nephron. Which of the following agents is the best choice for treatment of the hypertension and hypokalemic metabolic alkalosis in this patient?

A. amiloride
B. fludrocortisones
C. hydrochlorothiazide
D. lisinopril
E. spironolactone

Correct Answer: A
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Treatment of Liddle syndrome consists of direct inhibition of the abnormally expressed sodium channel by either amiloride (choice A) or triamterene, both of which are classified as potassium-sparing diuretics. Triamterene is less useful than amiloride because of its low potency and low solubility, which may lead to the

formation of stones. Fludrocortisone (choice B) is a synthetic mineralocorticoid used for replacement therapy in hypoaldosteronism. Although aldosterone levels are reduced in this patient, administration of a mineralocorticoid will exacerbate rather than relieve the hypertension and hypokalemic metabolic alkalosis. Hydrochlorothiazide (choice C), a thiazide diuretic, will exacerbate the problem because inhibition of the N /C symporter in the distal convoluted tubule results in

a^+

delivery of more sodium to the cortical collecting duct, where the hyperactivity of the sodium channel and resulting potassium extrusion along with increased proton exchange from type A intercalated cells results in greater hypokalemia and alkalosis. Lisinopril (choice D) is an ACE inhibitor used in the treatment of essential hypertension. Spironolactone (choice E) is a selective antagonist at the aldosterone receptor. It is used as a potassium-sparing diuretic. In the case of Liddle disease, spironolactone has no utility; aldosterone does not play a causative role and its levels are already depressed.

QUESTION 613
Which of the following correctly describes the mechanism of action of streptokinase?

A. combines with plasminogen to form an enzymatically active complex
B. competitively blocks binding of plasminogen to fibrin
C. converts plasmin to plasminogen
D. inhibits platelet cyclooxygenase (COX) activity
E. provides a template for combination of thrombin and antithrombin III

Correct Answer: A
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Streptokinase has no intrinsic enzymatic activity, but instead forms a stable complex with the patient's plasminogen, making it enzymatically active in cleaving free plasminogen to plasmin. The streptokinase plasminogen complex is not inhibited by antiplasmin. The other thrombolytic agents-- t-PA, reteplase, tenecteplase, and urokinase-- activate plasminogen directly. Competitive blocking of binding of plasminogen to fibrin (choice B) is a property of aminocaproic acid (AMICAR), a lysine analog used to inhibit fibrinolysis. Conversion of plasmin to plasminogen (choice C) is incorrect; it is plasminogen that is converted to plasmin in the thrombolytic action. Inhibition of cyclooxygenase activity (choice D) is a property of the NSAIDs that contributes to prevention of platelet aggregation and thrombosis. Heparin exerts its anticoagulant actions by providing a template for the combination of thrombin and antithrombin III (choice E).

QUESTION 614
A 17-year-old patient suffers from tonicclonic seizures. This condition has been well controlled with a regimen of phenytoin. Which of the following signs or symptoms indicates phenytoin toxicity?

A. diplopia and abnormal gait
B. hyperprolactinemia

C. polydipsia and polyuria
D. postural hypotension
E. rigidity and tremor

Correct Answer: A
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Diplopia, abnormal gait, and other signs of cerebellar dysfunction are important symptoms of phenytoin toxicity. Other manifestations of toxicity include gingival hyperplasia, nystagmus, and vertigo. Hyperprolactinemia (choice B) is an adverse effect of antipsychotic dopamine antagonists such as the phenothiazines; dopamine inhibits prolactin secretion by the anterior pituitary. Polydipsia and polyuria (choice C) are symptoms of diabetes insipidus. These symptoms may be produced by lithium toxicity during treatment of bipolar depression, and are not associated with phenytoin toxicity. Postural hypotension (choice D) is not an adverse effect of phenytoin but often occurs with levodopa treatment of Parkinson's disease. Rigidity and tremor (choice E) are symptoms of parkinsonism. These symptoms may be produced by dopamine antagonists such as antipsychotic agents, but are not associated with phenytoin toxicity.

QUESTION 615
Which of the following substances contains the highest concentration of molecules with estrogenic effects?

A. ginseng
B. grapefruit juice
C. kava
D. saw palmetto
E. tomatoes

Correct Answer: D
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Saw palmetto is promoted by purveyors of herbs and "alternative medicines" as therapy for prostatic hyperplasia and does have weak estrogenic activity. Ginseng (choice A) is known as an adaptogen, which means it increases resistance to physical, chemical, and biological stress and builds up energy and general vitality, including the mental and physical capacity for work. Grapefruit juice (choice B) and tomatoes (choice E) are used therapeutically in a treatment regimen referred to as "raw juice therapy." Raw juices of fruits and vegetables are extremely rich in vitamins, minerals, trace elements, enzymes, and natural sugars. Kava (choice C) is used in herbal therapy to treat anxiety, nervousness, nsomnia, stress, and restlessness. Only saw palmetto is known to have any estrogenic activity.

QUESTION 616
A 60-year-old man reports to the emergency room complaining of shortness of breath and a rapid, irregular heart beat. An ECG shows the pattern recorded in

below figure, panel A. Adiagnosis of atrial fibrillation, heart rate 140, is made. He is treated with an IV drug, which results in a change of the ECG, 1 hour after drug administration, to the pattern shown in panel B. This ECG was read as atrial fibrillation, heart rate 65. What drug was used?

A. adenosine
B. diltiazem
C. disopyramide
D. ibutilide
E. quinidine

Correct Answer: B
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
The initial atrial fibrillation ECG shows a very rapid ventricular rate, which decreases cardiac output and explains the patient's shortness of breath. After administration of the drug, the ventricular rate markedly slowed, but QRS duration and QT interval were not altered. This pattern of effects is observed with drugs that selectively slow AV conduction (i.e., beta blockers [antiarrhythmic group 2] and calcium channel blockers [group 4]). Adenosine (choice A) slows or blocks AV conduction but has a very short duration of action (seconds). Disopyramide (choice C) and quinidine (choice E) are group 1Aantiarrhythmic drugs and prolong the QRS and QT intervals. Ibutilide (choice D) is a group 3 drug and prolongs the QT interval. Cardiac glycosides such as digoxin also slow AV conduction (through their parasympathomimetic action), but have a slower onset of action than parenteral calcium channel blockers or beta blockers.

QUESTION 617
A patient with AIDS has bacterial meningitis and is being treated with an antimicrobial agent cleared by both hepatic metabolism and renal excretion. The volume of distribution is 10 L and the half-life for elimination is 7 hours in this patient. If the renal contribution to the plasma clearance of the drug is 8.3 mL/min, approximately what percentage of the drug's elimination can be attributed to hepatic metabolism?

A. 10%
B. 25%
C. 50%
D. 75%
E. 90%

Correct Answer: C
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
The total plasma clearance of the drug can be calculated from the relationship CL = 0.693 × Vd/ .

$t_{1/2}$

The total clearance is therefore 6.93 × 10 L/7 h or 0.99 L/h (which is equal to 16.5 mL/min). Because we know that the renal clearance is 8.3 mL/min, hepatic metabolism must account for the remaining 8.2 mL/min. Thus, hepatic metabolism accounts for about50% of the total drug elimination.

QUESTION 618
Calcium- and aluminum-containing antacids should be avoided by patients taking which of the following antimicrobial drugs?

A. amoxicillin
B. erythromycin
C. isoniazid
D. minocycline
E. rifampin

Correct Answer: D
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Tetracyclines such as minocycline chelate cations, such as aluminum and calcium, and may precipitate in the gut, greatly reducing antibiotic bioavailability. The other drugs listed (choices AC, E) have no significant interactions with antacids.

QUESTION 619

A young boy was treated for 2 years with several antibacterial agents to eradicate tuberculosis. On entering school the following year, his teacher reports that he seems to be retarded. Upon investigation, he is found to have profound hearing loss. Which of the following agents may have been responsible for this hearing loss?

A. ethambutol
B. isoniazid
C. pyrazinamide
D. rifampin
E. streptomycin

Correct Answer: E
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
The agents listed are the primary drugs used in the treatment of tuberculosis. Streptomycin (choice E) and other aminoglycosides cause eighth nerve damage, which is often irreversible and may take the form of auditory or vestibular dysfunction. Isoniazid and rifampin are the most efficacious and least toxic, but even when used together are insufficient in many cases to prevent the development of resistance. Therefore, most cases of tuberculosis are treated with three or even four agents in an effort to eradicate the infection before resistance develops. Because each drug has different toxicities, it is sometimes possible to achieve a cure without severe toxicity. Ethambutol (choice A) causes visual dysfunction and possible retinal damage, not hearing loss. Isoniazid (choice B) causes peripheral neuropathies and hepatic damage. Fortunately, hepatitis is uncommon in children treated with this drug. Pyrazinamide (choice C) causes joint pains and swelling, GI upset, and rash. Rifampin (choice D) causes proteinuria, rash, and thrombocytopenia.

QUESTION 620
Which of the following drugs exerts its effects through inhibition of cyclic GMP phosphodiesterase?

A. hydralazine
B. minoxidil
C. nitroprusside
D. prazosin

E. sildenafil

Correct Answer: E
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Vasodilators act by one of three mechanisms: increasing cyclic GMP (cGMP) levels in vascular smooth muscle cells; opening potassium channels; or blocking calcium channels. The organic nitrates and nitroprusside (nitrovasodilators) increase cGMP synthesis by generating nitric oxide (NO), which subsequently activates a soluble form of guanylyl cyclase. Activation of muscarinic receptors on vascular endothelial cells results in formation of NO (earlier identified as endothelium-derived relaxing factor) that diffuses to smooth muscle cells and relaxes them through increased cGMP levels. Erection of the penis involves neuronally regulated formation of NO, increased cGMP levels in the corpus cavernosum, and relaxation of cavernosal and vascular smooth muscle in erectile tissue. Rather than stimulating guanylyl cyclase, sildenafil (Viagra) acts as a selective inhibitor of cGMP phosphodiesterase type 5 to increase the half-life of cGMP in the tissues. The fact that sildenafil acts downstream of NO stimulation of guanylyl cyclase accounts for the toxic interactions between it and nitrovasodilators. The mechanism for relaxation of vascular smooth muscle by hydralazine (choice A) is unknown, but may involve NO. Minoxidil (choice B) is metabolized to minoxidil sulfate, which activates an ATP-sensitive potassium channel in smooth muscle. Nitroprusside (choice C) is a nitrovasodilator that spontaneously releases NO by a mechanism distinct from that of the organic nitrates. Prazosin (choice D) produces vasodilation by inhibiting alpha-1-adrenoreceptors on arteriolar smooth muscle.

QUESTION 621
A 57-year-old obese woman has Type II (noninsulindependent) diabetes mellitus of 15 years duration. Because her hyperglycemia is not well controlled with diet and oral hypoglycemic agents, she selfadministers insulin by injection. She comes to her physician's office with a fever and a draining external ear infection; Pseudomonas aeruginosa is cultured from the drainage fluid. Which of the following insulin regimens most closely mimics insulin release from a normally functioning pancreas?

A. prebreakfast and predinner injections of lente insulin plus an injection of regular insulin if blood glucose (measured by finger-stick) exceeds 150 mg/dL
B. premeal injections of insulin lispro plus morning and evening injections of detemir insulin
C. premeal injections of NPH insulin plus an injection of insulin lispro at bedtime
D. post-meal injection of lente insulin plus a prebreakfast injection of regular insulin
E. Post-meal injections of insulin glargine

Correct Answer: B
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Anormally functioning endocrine pancreas provides a low basal level of circulating insulin and spikes of insulin release in response to the ingestion of food and subsequent elevation of blood sugar. In a diabetic, use of morning and evening injections of a very long-acting form such as lente, glargine, or detemir insulin provides a low basal level of circulating insulin. Premeal injections of rapid-acting insulin provide the spikes of circulating insulin needed to deal with the dietary

glucose load. Regular insulin or insulin lispro, glulisine, or aspart is needed for this purpose. Insulin detemir and glargine are very long-acting recombinant insulins that are used to provide basal levels. They are of no value for controlling transient hyperglycemic spikes.

QUESTION 622
A 57-year-old obese woman has Type II (noninsulindependent) diabetes mellitus of 15 years duration. Because her hyperglycemia is not well controlled with diet and oral hypoglycemic agents, she selfadministers insulin by injection. She comes to her physician's office with a fever and a draining external ear infection; Pseudomonas aeruginosa is cultured from the drainage fluid. Which of the following drugs or drug combinations is appropriate treatment for the P. aeruginosa infection in this diabetic patient?

A. chloramphenicol
B. nafcillin plus kanamycin
C. sulfamethoxazole plus trimethoprim
D. tetracycline
E. ticarcillin plus tobramycin

Correct Answer: E
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
P. aeruginosa is an aerobic gram-negative bacterium that is frequently the causative agent in diabetic malignant external otitis. Increased susceptibility to infection in diabetics with poor glycemic control probably arises through impairment of leukocyte function. Such serious P. aeruginosa infections are best treated parenterally with a broad-spectrum beta-lactam cell wall synthesis inhibitor such as ticarcillin in combination with an aminoglycoside such as tobramycin. Chloramphenicol (choice A) is a protein synthesis inhibitor. P. aeruginosa is resistant to chloramphenicol. Nafcillin plus kanamycin (choice B) is a combination of a penicillinase-resistant penicillin plus a limitedspectrum aminoglycoside. Nafcillin is useful in treating penicillinase-producing staphylococcal infections, but does not possess a broadenough antibacterial spectrum to eradicate P. aeruginosa. Kanamycin is ineffective against P. aeruginosa and is used orally or topically, not parenterally as needed here. Sulfamethoxazole plus trimethoprim (choice C) is a combination of a folate synthesis inhibitor and a dihydrofolate reductase inhibitor that is effective in treating urinary tract infections. P. aeruginosa is resistant to this combination. Tetracycline (choice D) is a bacteriostatic protein synthesis inhibitor. When first introduced, tetracycline was effective in treating Pseudomonas, but now all strains are resistant.

QUESTION 623
A 20-year-old man suffers a broken arm in a bicycle accident. After a cast is applied, he is to be discharged from the emergency department with a prescription for an analgesic to be used if over-the- counter acetaminophen or nonsteroidal anti-inflammatory drugs (NSAIDs) are not effective in providing pain relief. Which of the following is the best choice for prescription pain relief in this case?

A. codeine
B. diphenoxylate
C. meperidine
D. methadone

E. morphine

Correct Answer: A
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Excellent analgesia and significant addictive properties are associated with drugs that act at mu-type opioid receptors. Of the analgesics listed, codeine is a weak agonist at mureceptors, whereas the other opioid analgesics listed (choices C, D, and E) are full agonists. Therefore codeine (choice A) is less efficacious but also has the lowest addiction and abuse liability; it is therefore the agent of choice within this list. Diphenoxylate (choice B) is a congener of meperidine (and the primary component of Lomotil) that is used to control GI motility in diarrhea. At therapeutic dose levels, neither analgesia nor addiction is observed. Meperidine (choice C) is a synthetic mu-opioid receptor agonist with high- addiction liability. Methadone (choice D) is a mu-opioid receptor agonist with good oral efficacy and a long plasma half-life (1540 h). It is used in the treatment of opioid addiction and for severe cancer pain. Morphine (choice E) is the prototype muopioid receptor agonist and possesses highaddiction liability.

QUESTION 624
On the basis of their mechanisms of action, which of the following combinations of drugs produces a beneficial additive or synergistic effect in therapy when each agent is present at its maximum effective concentration?

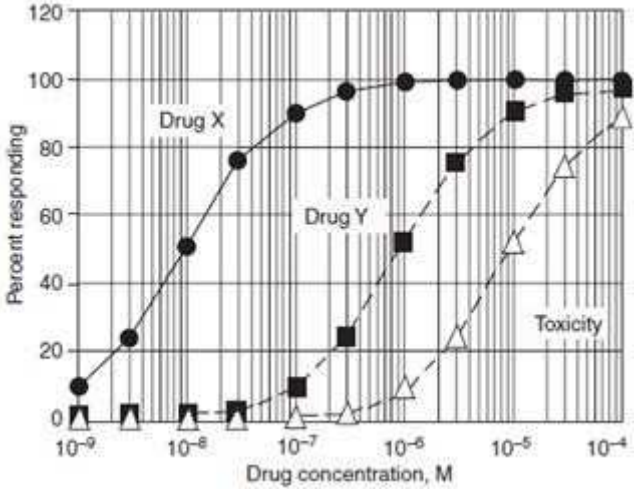
A. chlortetracycline plus amoxicillin
B. clomiphene plus chorionic gonadotropin
C. lovastatin plus cholestyramine
D. pentazocine plus morphine
E. succinylcholine plus atracurium

Correct Answer: C
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
The hydroxymethylglutaryl-CoA (HMGCoA) reductase inhibitor lovastatin and the bile acid-binding resin cholestyramine (choice C) lower the concentration of cholesterol in the blood by different mechanisms. Because they act by different mechanisms, combination therapy is at least additive. The combination of chlortetracycline and amoxicillin (choice A) results in antagonism of amoxicillin's antibacterial action. The beta-lactam cell wall synthesis inhibitors such as the penicillins and cephalosporins are bactericidal, but are effective primarily when the bacteria proliferate rapidly. Tetracyclines are bacteriostatic agents that slow or inhibit the growth of bacterial cells by inhibiting protein synthesis. The combination of clomiphene and chorionic gonadotropin (choice B) does not produce any beneficial additive action. Both agents are used to treat female infertility. Clomiphene is an estrogen-receptor partial agonist that functions at the level of the hypothalamus to stimulate release of gonadotropinreleasing hormone (GnRH). The increased release of GnRH results in increased release of the gonadotropins LH and FSH from the anterior pituitary. This results in stimulation of ovulation. Administration of chorionic gonadotropin also stimulates ovulation. Because both

preparations function through increases in gonadotropin levels and both are present at their maximum effective concentrations, a beneficial additive effect is unlikely. The combination of pentazocine and morphine (choice D) does not produce a beneficial interaction. Pentazocine exerts its pain-relieving activity by a weak (partial) agonist action at mu-opioid receptors. Morphine is a full agonist at the same receptors. When the two analgesic agents are combined, pentazocine acts as an antagonist for morphine at mu- receptors. The result is precipitation of withdrawal in addicted patients, and dysphoria and loss of morphine analgesia in nonaddicted patients. Succinylcholine and atracurium (choice E) are both skeletal musclerelaxing agents that block muscle contraction by actions at the neuromuscular junction. Succinylcholine is a depolarizing blocker that acts as an agonist at the nicotinic receptor. Atracurium is a competitive antagonist at the same receptor. Because they both act at the same receptor and are present at their effective concentrations, atracurium interferes with the action of succinylcholine.

QUESTION 625
Figure shows the quantal population doseresponse curves for the therapeutic and toxic effects of drugs X and Y. Both drugs are agonists at the same receptor to produce the therapeutic response, and the maximum responses obtained with each agent are the same. The toxicity curve in the figure shows the superimposed toxic response curves for drugs X and Y; they are identical in terms of the concentration dependence. Which of the following statements is most correct?



A. At 1 × 10-5 M both drugs cause adverse effects in 90100% of patients.
B. Drug X has a larger therapeutic index than drug Y.
C. Drug X is more efficacious than drug Y.
D. Drug Y is more potent than drug X.
E. Drug Y is safer than drug X.

Correct Answer: B
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Drug X has a larger therapeutic index (calculated as T /E) than drug Y. At a concentration of

D_{50}

1 × 1 M (choice A), both drugs produce adverse effects in about 50%, not 90100% of patients.

0^{-5}

Drug X is not more efficacious than drug Y (choice C); quantal doseresponse data provide no information about maximum efficacy and the question stem states that both drugs produce the samemaximum responses. Drug Yis not more potent than drug X (choice D); it is less potent (it has a higher E). Drug Y is not safer than drug X (choice E) from the data presented; if anything, more

C_{50}

adverse effects are produced by drug Y at its E than by drug X at its E .

C_{50}

QUESTION 626
A 78-year-old man has ankle edema, tachycardia, and shortness of breath on mild exercise. His blood pressure is 155/98. He has been diagnosed with hypertension and mild heart failure. Which of the following regimens is most appropriate for starting therapy?

A. captopril plus dobutamine
B. captopril plus hydralazine
C. enalapril plus hydrochlorothiazide
D. furosemide plus spironolactone
E. losartan plus hydralazine

Correct Answer: C
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
The combination of an ACE inhibitor and a diuretic is rational for this patient with hypertension and mild heart failure as both drugs are effective for both conditions. Furthermore, ACE inhibitors have been shown to slow or stop the progression of heart failure and thiazide diuretics have been shown to be among the cheapest

and most effective agents for hypertension. If this combination is not sufficiently active to control the heart failure, a loop diuretic mightbe substituted for the thiazide. Dobutamine (choice A) is a parenteral drug for acute failure. Hydralazine (choices B, E) is a vasodilator that causes tachycardia and usually requires concurrent administration of a beta blocker. Use of two diuretics choice D) is probably unnecessary in this early stage of failure and is not the most effective therapy for hypertension.

QUESTION 627
A 23-year-old woman is admitted to the hospital suffering from palpitations and syncopal episodes (fainting spells). She is found to be hypotensive and her ECG shows a very rapid AV nodal reentrant tachycardia. Which of the following drugs provides appropriate acute treatment for this condition?

A. adenosine
B. bethanechol
C. isoproterenol
D. metoprolol
E. procainamide

Correct Answer: A
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
The current drug of choice for acute AV nodal reentrant tachycardia (a supraventricular tachycardia [SVT]) is the nucleoside adenosine. This agent, when given as a bolus, causes marked hyperpolarization of AV node tissue and transiently blocks conduction of AV node action potentials. This abolishes the reentrant impulse and allows normal sinus rhythm to be reestablished. The half-life of adenosine is about 3 seconds and the duration of action of the dose used is about 15 seconds, so toxicities from this therapy are minimal. Calcium channel blockers such as verapamil and diltiazem are also effective in SVT. Bethanechol (choice B) is a muscarinic agonist and produces hypotension and other muscarinic effects. It is ineffective in SVT. Isoproterenol (choice C) is a beta-selective adrenoreceptor agonist that causes hypotension and reflex sympathetic discharge to the heart, along with direct stimulation. It is more likely to cause than to abolish arrhythmias. Metoprolol (choice D) slows AV conduction and might abolish the AV reentrant rhythm. However, beta blockers are not very effective in converting preexisting SVT. Procainamide (choice E) and related group 1A antiarrhythmic drugs are not as effective as adenosine in converting SVT to normal sinus rhythm and much more toxic.

QUESTION 628
A 38-year-old man has been treated for myasthenia gravis with pyridostigmine and propantheline for 8 years. He has had the "flu" for 10 days and his wife calls reporting that he now has serious muscle weakness. What should be administered after admitting this patient to the emergency department?

A. atropine to reverse the effects of an overdose
B. a test dose of edrophonium
C. pralidoxime on the assumption that he inadvertently overdosed
D. the daily dose of pyridostigmine on the assumption that he forgot to take his medication

E. tubocurarine

Correct Answer: B
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Myasthenia gravis is an autoimmune disease attributable to an impairment of nicotinic receptor function at the neuromuscular junction by antireceptor antibodies. Treatment consists of increasing the junctional concentration of acetylcholine with a carbamate anticholinesterase such as pyridostigmine. Infections such as influenza may change the anticholinesterase dose requirement in myasthenia either up or down. As in this patient, the problem is to distinguish whether the muscle weakness is attributable to myasthenic crisis (too little medication) or cholinergic crisis (too much medication); both conditions cause muscle weakness. The safest definitive method is to administer a small dose of the short-acting anticholinesterase edrophonium (choice B). If the patient is in myasthenic crisis, an immediate improvement in muscle function should be evident. If the patient is in cholinergic crisis, the patient's condition may worsen, but because the duration of action for edrophonium is only 510 min, this test provides less risk than other alternatives. Parenteral atropine should be available to treat excess parasympathetic activity. Atropine for symptoms of parasympathetic overdose (choice A) is inappropriate because this patient is being treated with the muscarinic antagonist propantheline and atropine will have no effect on his muscle weakness. Administration of pralidoxime (choice C) is incorrect because pralidoxime is useful for reactivation of cholinesterase only in the case of recent organophosphate intoxication. Administration of pyridostigmine (choice D) is unwise because a patient in cholinergic crisis is put at risk of exacerbation and extension of the toxic episode for a significant period of time. Administration of a test dose of a long-acting agent such as tubocurarine (choice E) to elicit muscle weakness is a provocative test that is dangerous and does not provide definitive evidence for diagnosis.

QUESTION 629
A 75-year-old man has prostate cancer that has metastasized to bone. He is receiving hormonal therapy to slow progression of the neoplasm and codeine by mouth for pain when it is absolutely required, but still complains of severe pain. What should be given to this patient to address his symptom?

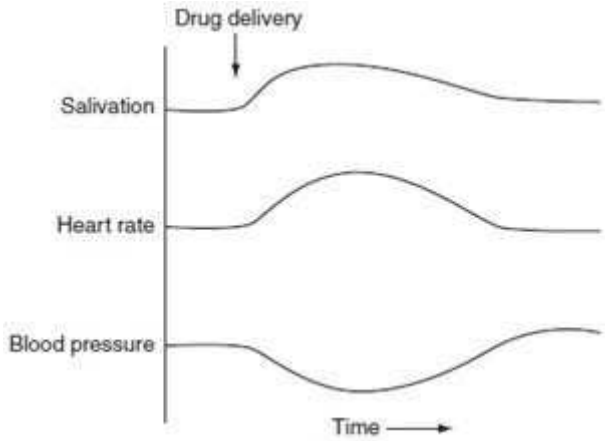
A. a strong NSAID such as naproxen as needed to supplement his codeine therapy
B. additional codeine when he complains
C. aspirin, and he should be told that additional narcotics cannot be used because he would become tolerant of their analgesic action
D. morphine in a long-acting oral preparation on a regular schedule and parenteral morphine when pain breaks through
E. parenteral morphine when pain requires it

Correct Answer: D
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Pain of malignancy is still a badly undertreated condition, due to misunderstanding of the nature of opioid tolerance and addiction and an unwillingness to deal with the complications of prescribing controlled substances. Codeine has limited maximum efficacy, so additional doses of this drug (choice B) are unlikely to control this patient's pain. It was previously thought that regular use of strong opioids for any purpose inevitably led to tolerance and a loss of analgesic effect, as well as

addiction (choice C). However, excellent clinical studies have shown that this is not the case. Regular use as opposed to as-needed use) of small to moderate doses of opioids effectively controls pain in most cases without causing tolerance or addiction. In fact, restricting opioids to use only when absolutely needed results in larger total analgesia requirements and greater toxicity. Use of NSAIDs (choice A) should be started early, when pain is mild and supplemented with oral opioids, such as codeine, as soon as it becomes necessary. NSAIDs are not adequate at this stage of this patient's disease. Parenteral morphine, given when necessary (choice E), is as not as effective as regularly scheduled morphine and leads to greater drug toxicity.

QUESTION 630
In a study of a new drug, the agent was administered to anesthetized animals while blood pressure, heart rate, and salivation were recorded. The results of a typical experiment are shown in below figure.
What is the best characterization of this new agent?



A. alpha-adrenoceptor agonist
B. alpha-adrenoceptor antagonist
C. cholinesterase inhibitor
D. direct-acting muscarinic agonist
E. ganglionic nicotinic agonist

Correct Answer: D
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Salivary glands contain muscarinic receptors, primarily of the M3 subtype, that receive parasympathetic innervation. Direct-acting agonists such as bethanechol and indirect agents such as neostigmine mimic parasympathetic nerve stimulation. Blood vessel endothelial cells contain M3 receptors that are not innervated, but

respond to circulating directacting muscarinic agonists. When these endothelial receptors are activated, nitric oxide synthesis is stimulated and smooth muscle relaxation occurs promptly with vasodilation and a drop in blood pressure. Because no nerve endings are present, indirect-acting cholinomimetics such as cholinesterase inhibitors do not have this vasodilating effect. In the presence of hypotension induced by a direct-acting muscarinic agonist, a strong compensatory reflex originates in the baroreceptors and results in tachycardia. In the case of cholinesterase inhibitors, the normal heart rate slowing effect of the vagus is amplified and at normal doses, bradycardia results. The effect of the new drug illustrated in figure is most consistent with a direct-acting muscarinic agonist (choice D). Alpha receptor ligands (choices A and B) have little effect on salivation, although indirectly acting agents like ephedrine can cause a sensation of dry mouth. However, ephedrine causes increased blood pressure. Aganglionic stimulant drug (choice E) causes increased salivation but also increases sympathetic discharge to the blood vessels and results in increased, not decreased, blood pressure.

QUESTION 631
Carbidopa is often used in patients with Parkinson's disease. Which of the following best describes the mechanism of action of carbidopa?

A. activates D2 receptors in the basal ganglia
B. inhibits the metabolism of dopamine in the blood and peripheral tissues
C. inhibits the metabolism of dopamine in the brain
D. inhibits the metabolism of levodopa in peripheral tissues
E. inhibits the metabolism of levodopa in the brain

Correct Answer: D
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Carbidopa is a peripheral inhibitor of dopa decarboxylase. Dopa decarboxylase is an enzyme present in large amounts in the GI tract and peripheral tissues, and in smaller amounts in the nerve terminals of dopaminergic neurons in the basal ganglia. It is required for the conversion of DOPA to dopamine in the biosynthesis of dopamine and norepinephrine. However, when the prodrug levodopa is used for parkinsonism, over 90% is metabolized in the periphery by the enzyme to dopamine and inactive products and only about 3% of the administered dose enters the brain. Because dopamine does not cross the bloodbrain barrier, dopamine formed outside the brain is of no value in treating parkinsonism. When carbidopa is given with levodopa, less levodopa is metabolized in the gut and other peripheral tissues, so more (about 10%) is available to enter the CNS. Carbidopa does not cross the bloodbrain barrier, so it does not prevent conversion of levodopa to active dopamine in the basal ganglia. Combination therapy thus reduces the peripheral effects of levodopadopamine and allows patients to receive more benefit and less toxicity from a given dose of levodopa. Choices AC and E are incorrect.

QUESTION 632
Which of the following is a recombinant human antibody used in advanced breast cancer?

A. adalimumab
B. etanercept
C. infliximab
D. sirolimus

E. trastuzumab

Correct Answer: E
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Trastuzumab is a human antibody that reacts with the epidermal growth factor receptor HER-2/neu and is effective in slowing progression of breast cancer. Adalimumab (choice A) and etanercept (choice B) are Ig antibodies to TNF-alpha and are used in advanced rheumatoid arthritis. Infliximab is a

G_1

chimeric antibody to TNF-alpha that is used in rheumatoid arthritis and several other autoimmune diseases. Sirolimus (choice D) is an inhibitor of B lymphocyte proliferation and immunoglobulin production. It is used to prevent transplanted organ rejection.

QUESTION 633
Exhibit:

A. cannabinoid receptor agonist
B. corticosteroid agonist
C. dopamine antagonist
D. H_1 histamine antagonist
E. serotonin 5-HT_3 antagonist

Please refer to the exhibit.
Apatient is to receive chemotherapy for cancer. The oncologist plans to use ondansetron to reduce the nausea and vomiting associated with the chemotherapeutic agents. What is the mechanism of action of ondansetron?

A. A
B. B
C. C
D. D
E. E

Correct Answer: E
Section: Pharmacology

Explanation

Explanation/Reference:
Explanation:
All of the mechanisms listed are valid mechanisms of antiemetic drugs that are used in cancer chemotherapy. Ondansetron is a 5-H antagonist. Dronabinol is a cannabinoid agonist (choice A).

T_3

Dexamethasone is a corticosteroid (choice B). Metoclopramide is a dopamine antagonist (choice C). Diphenhydramine is a histamine antagonist (choice D). In the prevention of nausea and vomiting caused by chemotherapeutic agents, a cocktail of three, four, or more of these agents is often used. ndansetron is also effective in reducing postsurgical vomiting. Several congeners of ondansetron are available (granisetron, dolasetron).

QUESTION 634
Which of the following associates the correct mechanism of action with a drug used in Type II (noninsulin-dependent) diabetes?

A. acarbose--reduction of insulin resistance
B. glipizide--inhibition of intestinal alphaglucosidase
C. metformin--inhibition of ATP-sensitive potassium channels
D. repaglinide--modulation of pancreatic insulin release
E. rosiglitazone--reduction in circulating glucagon levels

Correct Answer: D
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Pancreatic beta cells are electrically polarized. Depolarization causes entry of calcium and activation of insulin exocytosis. In hypoglycemia, the negative resting potential is maintained by the activity of an ATP-sensitive hyperpolarizing potassium channel and insulin secretion is inhibited. When extracellular glucose levels are high, glucose enters the beta cells via the GLUT2 transporter and is metabolized to yield ATP. The increased ATP levels cause closure of the potassium channel, allowing the cell to depolarize and secrete insulin. Modulation of insulin release (choice D) is the mechanism of action of the meglitinides such as repaglinide. Although the details are not fully understood, these drugs share one binding site with sulfonylureas and have a second, independent binding site. Acarbose (choice A) is an inhibitor of intestinal alpha-glucosidase and thus reduces absorption of glucose. Sulfonylureas such as glipizide (choice B) bind to a cell-surface protein to cause inhibition of the hyperpolarizing potassium channel, thereby allowing the beta cell to depolarize and secrete insulin. Metformin (choice C) and other biguanides are poorly understood, but do not inhibit the potassium channel that is the target of sulfonylureas. Rosiglitazone (choice E) and pioglitazone do not act by reduction of circulating glucagon; this is one proposed mechanism for the biguanides. These thiazolidinediones or "glitazones" appear to act by a peripheral mechanism that reduces insulin resistance, probably mediated by the peroxisome proliferator-activated receptor-gamma (PPAR-gamma) nuclear receptor.

QUESTION 635
The table below provides several possible descriptions of the actions of nondepolarizing neuromuscular blockers such as tubocurarine. Which description is most accurate?

Choice	Effect of Tetanic Stimulation	Posttetanic Potentiation	Reversal by Neostigmine
A	Fade	No	No
B	Constant	Yes	No
C	Fade	No	Yes
D	Fade	Yes	Yes
E	Constant	Yes	Yes

A. Option A
B. Option B
C. Option C
D. Option D
E. Option E

Correct Answer: D
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Nondepolarizing neuromuscular blockers are heavily used in anesthesia because they produce full surgical relaxation without causing significant cardiovascular depression. They act as nicotinic cholinoceptor blockers at the neuromuscular nicotinic receptor, with little or no ganglionic blockade. They have some effect on presynaptic cholinoceptors of motor nerves and it is believed that this site of action is the cause of alterations in the response of the motor nervemuscle system to rapid stimulation. A train of four stimulations, a form of titanic stimulation, is used by anesthesiologists to monitor the level of neuromuscular block in the anesthetized patient and consists of a brief period of stimulation. In the absence of drugs, as well as in the presence of a depolarizing blocker, the twitches during train of four are well maintained in strength. However, after a nondepolarizing blocker the contraction strength fades during the sequence (choices A, C, or D). In the absence of drugs, rapid tetanic stimulation results in moderate increase in contraction during the tetanus and a marked increase in strength of the muscle twitch following the end of the train due, at least in part, to a buildup of calcium in the motor nerve terminal. This posttetanic potentiation is enhanced by nondepolarizing blockers (choices B, D, or E). Finally, nondepolarizing blockade results from competitive blockade of cholinoceptors, so increasing the amount of acetylcholine in the synapse by means of a drug like neostigmine can reverse the blockade (choices C, D, or E). Thus, only choice D meets all three requirements.

QUESTION 636
Which of the following agents is most effective as a cardiac stimulant in the treatment of severe beta- blocker overdose?

A. atrial natriuretic peptide
B. epinephrine
C. glucagon
D. human growth hormone
E. insulin

Correct Answer: C
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
The cardiac manifestations of beta-blocker intoxication can be very severe, resulting in bradycardia, AV blockade, and markedly reduced force of contraction and cardiac output. Hypotension is common. However, the heart has glucagon receptors that are linked to stimulation of adenylyl cyclase independent of beta adrenoreceptors, which mediate marked increases in rate and force and substitute for the blocked beta response. (Glucagon also plays a primary role in raising blood glucose levels through activation of glycogenolysis and gluconeogenesis.) Atrial natriuretic peptide (choice A) is released from the cardiac atria and causes vasodilation through activation of membranebound guanylyl cyclase in arteriolar smooth muscle, and sodium excretion in the urine through an increase in glomerular filtration rate and consequent increase in filtration fraction. It is of no value in beta-blocker overdose. If the beta-blocker overdose is sufficient, administration of beta agonists such as epinephrine (choice B) is inadequate to overcome the blockade. Human growth hormone (choice D) is a peptide hormone produced by the anterior pituitary. It stimulates growth at open epiphyses through production of the insulin-like growth factors. It has no direct effect on cardiac function. Insulin (choice E) activates entry of glucose into most tissues and promotes glycogen and triglyceride storage. It has no direct effects on cardiac function.

QUESTION 637
At a blood alcohol level of 200 mg/dL (0.2%), which of the following correctly describes the systemic elimination process for ethanol?

A. constant clearance via liver, kidney, and lungs
B. first-order elimination via pulmonary exhalation
C. first-order elimination via renal excretion
D. second-order elimination via biliary secretion
E. zero-order elimination via hepatic metabolism

Correct Answer: E
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
At a blood alcohol level of 200 mg/dL, most individuals are grossly inebriated; a level of 80100 mg/dL (0.080.1%) is considered the legal threshold for intoxication in

most states. Ethanol is metabolized by alcohol dehydrogenase (and to a lesser extent by the microsomal ethanol oxidizing system) to acetaldehyde, primarily in the liver. At most ethanol concentrations, the metabolizing system is saturated. As a result, zeroorder kinetics are observed. A typical adult shows a constant elimination rate manifested as a decline in blood level of 1622 mg/dL/h. As blood alcohol levels drop below about 100 mg/dL, elimination has characteristics intermediate between zero and first order. Only at concentrations below 1 mg/dL is the elimination truly first order. Constant clearance (choice A) requires first-order elimination. Pulmonary excretion (choice B) of ethanol accounts for only a minor component of elimination. Breath analyzers are used to estimate the blood alcohol level in drivers suspected of driving under the influence of alcohol. Renal excretion (choice C) also accounts for only a minor component of systemic elimination of alcohol. Because of the small size of the ethanol molecule, most of the alcohol undergoing filtration at the glomerulus is reabsorbed. Biliary secretion (choice D) is not significant in ethanol elimination. At a concentration of 200 mg/dL, blood alcohol is eliminated at zero-order kinetics via hepatic alcoholic dehydrogenase.

QUESTION 638
The following are pharmacokinetic data for the drug propranolol in a 70-kg person: clearance, 50 L/h; volume of distribution, 270 L; effective plasma concentration, 20 ng/mL; oral availability (percentage), 25%. What is the oral maintenance dosing rate for propranolol in a 70-kg person?

A. 10 g/h
B. 200 g/h
C. 1 mg/h
D. 4 mg/h
E. 54 mg/h

Correct Answer: D
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
The maintenance dosing rate (D/T) is calculated using the formula D/T = target × CL/F, where D is the dose administered, T is the time interval between doses, the target is the desired steady-state plasma concentration (for which the effective plasma concentration is used), CL is the systemic clearance, and F is the fractional absorption. After multiplying the clearance (50 L/h) times the effective plasma concentration (0.02 mg/L), the resulting product of 1 mg/h must be divided by the fractional absorption of 0.25, giving a dosing rate of 4 mg/h. Note that the units for clearance and target concentration must be consistent with respect to volume. The extensive first-pass metabolism of propranolol means that to achieve the same systemic concentration, an oral dose four times larger than the IV dose must be administered.

QUESTION 639
A 72-year-old woman is brought to the clinic by her family because she is exhibiting confusion. Upon mental status examination, the patient demonstrates fluctuating levels of awareness. For example, she seems lucid 1 minute, then becomes somnolent or stuporous the next. Which of the following is most likely?

A. delirium
B. dementia

C. factitious illness
D. malingering
E. stupor

Correct Answer: A
Section: Behavioral Science and Biostatics
Explanation

Explanation/Reference:
Explanation:
Fluctuating levels of awareness are characteristic of delirium, which is indicative of an encephalopathy due to metabolic derangement of the brain, such as anoxia, electrolyte imbalance, or hypoglycemia. Although delirium may be superimposed on dementia, at this point there is no evidence that the patient has the more stable cognitive deficits characteristic of dementia (choice B). Coma (choice D) and stupor (choice E) refer to more severe disturbance of sensorium. Factitious illness (choice C) is unlikely unless there is evidence of selfinduced metabolic derangement.

QUESTION 640
An elderly patient, known to suffer from dementia, was found walking aimlessly in the fields in hot weather for several hours before being brought to the clinic. Which of the following would be the most useful laboratory test?

A. electrocardiogram
B. electroencephalogram
C. pneumoencephalogram
D. serum electrolyte levels
E. urinalysis

Correct Answer: D
Section: Behavioral Science and Biostatics
Explanation

Explanation/Reference:
Explanation:
An elderly woman exposed to hot sunlight for hours may be dehydrated, and testing serum electrolyte levels may confirm this suspicion. Although the other tests (choices A, B, C, and E) may be indicated at some point, they are not the most urgent tests in this case.

QUESTION 641
A family reports that their mother's mental status has been deteriorating for the past several years, during which time she has had episodes of transient weaknesses of the arms and legs. Which of the following is the most likely diagnosis?

A. Alzheimer's disease

B. Korsakoff syndrome
C. multi-infarct dementia
D. old age
E. vitamin deficiency

Correct Answer: C
Section: Behavioral Science and Biostatics
Explanation

Explanation/Reference:
Explanation:
Multi-infarct dementia is caused by repeated cerebrovascular ischemia, indicated in this case by periods of transient paralysis. Alzheimer's disease (choice A) is the most common primary dementia in the elderly. Old age (choice D) alone is no cause for dementia. Korsakoff syndrome (choice B), which is characterized by confabulation, is associated with alcohol withdrawal and thiamine deficiency (choice E). There is no evidence of either in this case.

QUESTION 642
Which of the following is an id function?

A. aggression
B. cognition
C. conscience
D. perception
E. psychological defense mechanisms

Correct Answer: A
Section: Behavioral Science and Biostatics
Explanation

Explanation/Reference:
Explanation:
The id is the collection of psychological functions having to do with basic instincts, such as sex and survival. Aggression is a basic instinct, therefore, an id function. The ego functions to mediate between the personality system on one hand and the demands of external reality and the superego on the other hand. Thus, psychological defense mechanisms (choice E), perception (choice D), and cognition (choice B) are all ego functions. Superego is the part of the personality system that encompasses conscience (choice C).

QUESTION 643
Your patient reports being frightened by heart palpitations and dizziness. Further evaluation reveals that the patient has used a substance heavily, but stopped about 3 days prior to experiencing symptoms, which of the following is the most likely substance used?

A. alprazolam
B. cannabis
C. cocaine
D. dextroamphetamine
E. heroin

Correct Answer: A
Section: Behavioral Science and Biostatics
Explanation

Explanation/Reference:
Explanation:
Benzodiazepine withdrawal is often associated with anxiety symptoms. Cocaine (choice C) may cause a "crash" with anxiety soon after cessation of use, but by day 3 there is more likely to be dysphoria than anxiety. Although withdrawal from other substances (choices B, D, and E) can cause similar anxiety, benzodiazepine withdrawal is the most common cause of this type of symptomatology

QUESTION 644
Your patient reports that she is suffering from dizziness and persistent feelings that she is going to die. You inquire as to whether she has been using any illicit substances lately to which she indicates that she has not. She indicates that she has been curtailing going outside, especially in open spaces, because she is afraid that she might have one of those attacks and become immobilized, which of the following is the most likely diagnosis?

A. acute anxiety attack
B. agoraphobia with panic attack
C. agoraphobia without panic attack
D. anxiety secondary to a medical condition
E. cocaine withdrawal

Correct Answer: B
Section: Behavioral Science and Biostatics
Explanation

Explanation/Reference:
Explanation:
The symptoms of panic associated with fear and avoidance of being in places where escape may be difficult or embarrassing call for the consideration of agoraphobia with panic attack. Choices A, C, D, and E are not associated with the phenomenon described here.

QUESTION 645
Which of the following implies the multiaxial diagnostic system in psychiatric disorders?

A. All psychiatric disorders are personality disorders.
B. Psychiatric disorders and other diseases can coexist.
C. Psychiatric disorders are a subset of medical diseases.
D. Psychiatric disorders are complex.

Correct Answer: B
Section: Behavioral Science and Biostatics
Explanation

Explanation/Reference:
Explanation:
Axis I of the multiaxial system is for clinical psychiatric disorders such as schizophrenia and mood disorders. Axis II is for personality disorders and mental retardation. Axis III is for general medical conditions (such as myocardial infarction). Axis IV is for psychosocial and environmental problems and Axis V is for global assessment of functioning. This classificatory system clearly indicates that psychiatric disorders (Axis I) and general medical disorders (Axis III) often do coexist and may influence each other. Choices A, C, and D are not part of the multiaxial system.

QUESTION 646
A 72-year-old man is discovered wandering in the hot sun by hospital staff several hours after being reported missing. Recommended testing involves analysis of serum electrolytes. The assay revealed the following serum values: Na+ 150 mEq/L, K+ 5.2 mEq/L. Which of the following is the most likely diagnosis?

A. Alzheimer's disease
B. delirium
C. lewy body dementia
D. secondary dementia
E. seizure disorder

Correct Answer: B
Section: Behavioral Science and Biostatics
Explanation

Explanation/Reference:
Explanation:
The hypernatremia and hyperkalemia are indicative of dehydration, which is a common cause of delirium. Choices A, C, D, and E do not explain this phenomenon.

QUESTION 647
Which of the following is the most characteristic element of managed care?

A. Capitated payment.
B. That it emphasizes prevention and health promotion.

C. That it is a fee-for-service system.
D. That it provides primary care.
E. That physicians may be salaried.

Correct Answer: A
Section: Behavioral Science and Biostatics
Explanation

Explanation/Reference:
Explanation:
Managed care involves an entity (company, state, organization) managing health care through a capitated (head count) payment system. Within the managed care system, there are various models including specialized care and fee for service in addition to capitation.

QUESTION 648
Which of the following statements is true concerning infant mortality in the United States?

A. Infant mortality in the United States is high compared to other developed nations.
B. Prenatal care, disappointingly, has not been shown to reduce infant mortality.
C. The leading cause of infant mortality in the United States is tetanus.
D. The mortality rate for white infants is greater than that of black infants.
E. Very few Asian Americans receive prenatal care as compared to African Americans or Hispanic Americans.

Correct Answer: A
Section: Behavioral Science and Biostatics
Explanation

Explanation/Reference:
Explanation:
The infant mortality rate in the United States is 8.9 deaths per 1000 live births as of 1989, which ranks the United States behind 11 other developed countries. The leading causes of infant death are congenital anomalies, respiratory distress syndrome, and sudden infant death syndrome; therefore, choice C is incorrect. Choices B, D, and E are incorrect because prenatal care does reduce infant mortality, but only 80% of Caucasian women receive prenatal care, followed by 75% of Asian American women, 65% of African American women, and 60% of Native American women. The infant mortality rate for black infants is greater than that of white infants.

QUESTION 649
Taking a careful history of a 20-year-old female patient suffering from dissociative identity disorder is likely to reveal which of the following?

A. a history of criminal behavior during childhood
B. an excellent school record

C. physical or sexual abuse in childhood
D. setting of fires in childhood

Correct Answer: C
Section: Behavioral Science and Biostatics
Explanation

Explanation/Reference:
Explanation:
Dissociative identity disorder (multiple personality disorder) is often associated with a history of severe emotional, physical, or sexual abuse in childhood. The dissociation may serve an adaptive function that enables the patient to tolerate an intolerable situation. The patient's school record is often poor due to memory disturbance associated with the disorder. Choices A and D are associated with antisocial personality, and choice A is unlikely because dissociation often causes inattention and poor school grades.

QUESTION 650
Which of the following is the earliest developmental phase according to Piaget?

A. concrete operations
B. formal operations
C. Oedipus complex
D. preoperational phase
E. sensorimotor period

Correct Answer: E
Section: Behavioral Science and Biostatics
Explanation

Explanation/Reference:
Explanation:
Piaget described the development of intelligent thinking in stages. The first is the sensorimotor period, 18 months2 years. This is followed by preoperational phase, 27 years (choice D); and the phase of concrete operations, 711 years (choice A), and the period of formal operations from adolescence through adulthood (choice B). Oedipus complex (choice C) is not a Piagetian stage, but is characteristic of ages 35.

QUESTION 651
According to Erikson, which of the following is a major developmental task for most children around 15 years of age?

A. developing a clear identity
B. developing a sense of integrity
C. developing intimate relationships

D. learning about sex
E. learning to be independent

Correct Answer: A
Section: Behavioral Science and Biostatics
Explanation

Explanation/Reference:
Explanation:
Erikson describes adolescence as the period of identity formation. In this period, a person develops a sense of inner sameness and continuity, a sense of direction and self. Career choices are also made during this phase. Failure of identity formation in this period results in "role confusion." Choices B and C refer to other developmental periods or non-Eriksonian task (choice D & E).

QUESTION 652
An elderly patient with multi-infarct dementia also suffers from urinary incontinence and ataxia. Which of the following therapeutic procedures may be considered for this type of patient?

A. benzodiazepines
B. electroconvulsive therapy
C. megavitamin therapy
D. urocholine
E. ventriculoperitoneal shunt

Correct Answer: E
Section: Behavioral Science and Biostatics
Explanation

Explanation/Reference:
Explanation:
Normal pressure hydrocephalus is associated with the symptoms of dementia, ataxia, and urinary incontinence. On brain imaging, the ventricles are often enlarged, but cerebrospinal fluid (CSF) pressure is normal. Aventriculoperitoneal shunt is often therapeutic for this condition. Choices A, B, C, and D are inappropriate.

QUESTION 653
All patients who have trisomy of autosome 21 who survive to adulthood develop which one of the following conditions?

A. Alzheimer's disease
B. lewy body dementia
C. multi-infarct dementia
D. Pick disease

E. secondary dementia

Correct Answer: A
Section: Behavioral Science and Biostatics
Explanation

Explanation/Reference:
Explanation:
Down syndrome is a congenital mental retardation associated with trisomy of autosome 21. All patients with Down syndrome who survive into adulthood develop the brain pathologies of Alzheimer's disease, rendering support to the notion that at least one form of Alzheimer's disease may be associated with an autosome 21 abnormality. Choices B, C, D, and E are not associated with trisomy of autosome 21.

QUESTION 654
Which of the following is the most treatable dementing disease?

A. Alzheimer's disease
B. Creutzfeldt-Jakob disease
C. multi-infarct dementia
D. Pick disease
E. Wernicke syndrome

Correct Answer: E
Section: Behavioral Science and Biostatics
Explanation

Explanation/Reference:
Explanation:
Wernicke syndrome is caused by thiamine deficiency associated with alcohol withdrawal, and can be treated effectively. Alzheimer's disease (choice A) is the most common primary dementia in the elderly. About 50% of brains of demented patients show evidence of Alzheimer's disease. Creutzfeldt- Jakob (choice B) disease and kuru are slow virus infections that show clinical and histologic features similar to Alzheimer's disease. Multiinfarct dementia (choice C) is secondary to repeated cerebrovascular accidents (CVAs) in patients with underlying atherosclerosis or hypertension. It is more common among men than women. Pick disease (choice D) is a rare cause of cortical dementia. The presence of unilateral cortical atrophy in Pick disease contrasts with the bilateral atrophy evident in Alzheimer's disease. Microscopically, Pick bodies composed of densely packed neurofilaments are seen within diseased neurons.

QUESTION 655
Which of the following is the most common type of substance dependency in the United States?

A. alcohol
B. cannabis

C. cocaine
D. heroin
E. tobacco

Correct Answer: E
Section: Behavioral Science and Biostatics
Explanation

Explanation/Reference:
Explanation:
Tobacco addiction is the most common type of drug dependency in the United States. Nicotine is extremely addictive. Since the Surgeon General's report in 1964 that identified the health risks of tobacco smoking, there has been an encouraging trend in the United States. Approximately 42% of the US adult population smoked cigarettes in 1965. The rate was 37% in 1975 and 30% in 1985. The reduction rate of smoking has been more pronounced in males than in females. Choices A, B, C, and D are incorrect.

QUESTION 656
A 52-year-old woman tells her doctor that she is experiencing pains in the abdomen and thighs and insists that she is suffering from some form of cancer. A physical examination reveals only the presence of extensive varicose veins. While collecting additional patient history, you find that the woman has become increasingly anxious, with a sense of impending doom, and intensifying abdominal discomfort. You decide to do further medical workup to rule out cancer. Which of the following malignancies is most likely in this patient?

A. carcinoma of the pancreas
B. glioblastoma
C. carcinoma of the stomach
D. Kaposi sarcoma
E. pancoast tumor

Correct Answer: A
Section: Behavioral Science and Biostatics
Explanation

Explanation/Reference:
Explanation:
Carcinoma of the tail of the pancreas often presents with symptoms of depression. Although other carcinomas and neoplasms (choices B, C, D, and E) may also cause depression, pancreatic cancer has to be ruled out first in a patient with severe depression.

QUESTION 657
Which of the following ratios represents the estimated likelihood that a physician will become addicted to narcotics during his/her career?

A. 1 in 10
B. 1 in 100
C. 1 in 1000
D. 1 in 10,000
E. 1 in 100,000

Correct Answer: B
Section: Behavioral Science and Biostatics
Explanation

Explanation/Reference:
Explanation:
Because of easy drug availability and their high-stress occupation, physicians are at high risk for narcotic drug addiction; the incidence is estimated to be 1 in 100, which is 30 to 100 times greater than that of the general population. Choices A, C, D, and E are incorrect.

QUESTION 658
Which of the following has a triphasic abstinence syndrome, the first phase being the "crash"?

A. alcohol
B. barbiturates
C. cannabis
D. cocaine
E. opiates

Correct Answer: D
Section: Behavioral Science and Biostatics
Explanation

Explanation/Reference:
Explanation:
The abstinence syndrome to cocaine is triphasic. Phase 1 is called "crash," phase 2 is a withdrawal phase with protracted dysphoria, and phase 3 is an "extinction" phase that follows the resolution of withdrawal anhedonia. Choices A, B, C, and E do not show this type of triphasic syndrome.

QUESTION 659
The activity of which structure in the pons is suppressed by opioids, alpha-2-agonists, and gammaaminobutyric acid (GABA), and produces most of the noradrenergic input to the brain?

A. anterior Cingulate Gyrus
B. locus ceruleus

C. mammillary bodies
D. nucleus pulposus
E. nucleus solitarius

Correct Answer: B
Section: Behavioral Science and Biostatics
Explanation

Explanation/Reference:
Explanation:
The locus ceruleus, located in the pons, produces most of the noradrenergic input to the brain, and has receptors for opioids and autoreceptors for norepinephrine (á-2) as well as GABA. The locus ceruleus seems to be involved in alertness and anxiety response. Choices A, C, D, and E refer to structures elsewhere.

QUESTION 660
Unmyelinated C fibers are thought to carry which of the following pain sensations?

A. aching
B. burning
C. dull
D. gnawing
E. pricking

Correct Answer: B
Section: Behavioral Science and Biostatics
Explanation

Explanation/Reference:
Explanation:
It is now believed that specific pain receptors (free nerve endings) are stimulated mainly by chemicals such as bradykinin, and that two types of pain sensations ("pricking" and "burning") are transmitted by different types of nerves. The burning pain sensation is transmitted by small C-fibers, and the pricking pain sensation is transmitted by larger, myelinated A-delta fibers. The pain fibers eventually terminate in the thalamus in a somatotopical fashion. Choices A, C, D, and E are incorrect.

QUESTION 661
Which theory concerning pain postulates that non-pain sensations, such as vibration or pressure, may affect the transmission and perception of pain sensation?

A. bradykinin theory
B. gate control theory
C. pattern theory

D. peptide theory
E. specificity theory

Correct Answer: B
Section: Behavioral Science and Biostatics
Explanation

Explanation/Reference:
Explanation:
The theories involving pain perception are: (1) the specificity theory (choice E), postulating that there are specific pain receptors transmitting specific pain signals through specific neurons to specific areas of the brain; (2) the pattern theory (choice C), postulating the existence of "reverberating circuits" to explain phantom pain; and (3) the gate control theory (choice B), postulating an interaction between pain sensation and other sensations competing for transmission at the spinal cord level. Choices A and D do not postulate the interaction with non-pain sensations.

QUESTION 662
Aphysician is treating a patient whom he suspects of factitious disorder. If the physician learns that the patient would have been incarcerated for a criminal offense if he had not been hospitalized, which of the following diagnoses becomes most likely?

A. antisocial personality disorder
B. borderline personality disorder
C. malingering
D. Munchausen syndrome
E. sick-role addiction

Correct Answer: C
Section: Behavioral Science and Biostatics
Explanation

Explanation/Reference:
Explanation:
When there is an external incentive for causing the symptom or injury, malingering is more likely than factitious disorder (Munchausen syndrome), the motivation for which is often quite unclear. Although there may be concomitant personality disorders, malingering is not diagnostic of any specific personality disorder. Choices A, B, D, and E are less likely because there seems to be an obvious and conscious motivation in this case.

QUESTION 663
A patient has begun exhibiting signs of paranoia and psychosis within the past week. In considering the diagnosis of schizophrenia, which of the following is a crucial piece of information?

A. The patient does not smoke.

B. The patient has a history of similar psychotic episodes in the past.
C. The patient has a history of substance abuse.
D. The patient is a toxicologist.
E. The patient is single.

Correct Answer: B
Section: Behavioral Science and Biostatics
Explanation

Explanation/Reference:
Explanation:
Although all the other items (choices A, C, D, and E) may be significant, schizophrenia cannot be diagnosed if the patient has never had an episode of psychotic symptoms lasting for at least 6 months.

QUESTION 664
A 25-year-old man is admitted to the hospital after coming to the doctor carrying a bottle containing bloody urine. All tests were negative, and he was observed stealing a test tube of blood from the laboratory technician's cart. Which of the following is the most likely diagnosis?

A. antisocial personality disorder
B. factitious disorder
C. malingering
D. schizophrenia
E. somatization disorder

Correct Answer: B
Section: Behavioral Science and Biostatics
Explanation

Explanation/Reference:
Explanation:
The essential feature of factitious disorder is the intentional production of physical signs or symptoms in the absence of an external incentive as a motivation. If there is an external incentive for fabricating an illness, then malingering is diagnosed (choice C). Antisocial personality disorder (choice A) requires a pattern of antisocial behavior. Somatization disorder (choice E) is characterized by multiple physical symptoms that are not explained by tissue damage. Schizophrenia (choice D) is incorrect because there is no evidence of psychotic symptoms even though the behavior may be bizarre.

QUESTION 665
A 48-year-old woman comes to the doctor complaining of vague pains in the abdomen, legs, and thighs. On physical examination, the only positive findings are varicose veins of 20 years' duration. The patient, upon being told of this, insists on being operated on for the varicose veins immediately. Which of the following is most likely to underlie this wish for immediate surgery?

A. anxiety
B. depression
C. drug dependence
D. psychosis

Correct Answer: A
Section: Behavioral Science and Biostatics
Explanation

Explanation/Reference:
Explanation:
Anxiety or concomitant stress is a common trigger for help-seeking behavior, especially if the symptom or sign is of long duration. Although depression (choice B) can cause vague discomfort and precipitate help seeking, insisting on an operation immediately seems to indicate anxiety rather than depression, which is more likely to cause indecision or inaction. A drug-dependent person (choice C) is more likely to insist on drugs. There is no evidence of psychosis (choice D).

QUESTION 666
Your patient is convinced that she has cancer. She is clearly agitated and is complaining of pain in her abdomen. A workup for cancer is negative, yet your patient refuses to accept the diagnosis and becomes increasingly anxious and expresses an intense sense of impending doom. Which of the following drugs is most appropriate for the treatment of this patient?

A. carbamazepine
B. methylphenidate
C. olanzapine
D. paroxetine
E. valproic acid

Correct Answer: D
Section: Behavioral Science and Biostatics
Explanation

Explanation/Reference:
Explanation:
Paroxetine is a selective serotonin reuptake inhibitor (SSRI), an antidepressant, and is the drug of choice for treating this patient's depression. Carbamazepine (choice A), like valproic acid (choice E), is an anticonvulsant and mood stabilizer which may be used to treat bipolar disorder. Methylphenidate (choice B) is a CNS stimulant; olanzapine (choice C) is an atypical antipsychotic.

QUESTION 667
Ayoung woman presents to the physician with the chief complaint of palpitations. She also complains of feelings that she is going to die, with feelings of dizziness.

Which of the following is the most useful question to ask?

A. Are you anxious?
B. Do you have a heart disease?
C. Has anything like this happened before?
D. What drugs do you use?
E. Why do you think you will die?

Correct Answer: C
Section: Behavioral Science and Biostatics
Explanation

Explanation/Reference:
Explanation:
The patient presents with acute anxiety symptoms that might be due to panic or other acute situations. Panic disorder usually is recurrent and history of previous episodes would be extremely helpful. Choice A is inappropriate; the patient is obviously anxious. Choices B, D, and E may be useful but not yield as much information.

QUESTION 668
If laboratory tests determine that the patient has a general medical condition that underlies the symptoms, which of the following is most likely?

A. Addison disease
B. cancer of the pancreas
C. hyperparathyroidism
D. hyperthyroidism
E. hypothyroidism

Correct Answer: D
Section: Behavioral Science and Biostatics
Explanation

Explanation/Reference:
Explanation:
Hyperthyroidism is often associated with anxiety and panic symptoms. Although these symptoms may also occur with any of the other medical conditions (choices A, B, C, and E), depression and slowed mentation are more common in hypothyroidism, hyperparathyroidism, and Addison disease; cancer of the pancreas is often associated with severe depression.

QUESTION 669
Sean is 8 years old. He is referred by his school because he is habitually disruptive in class. Which of the following is the most useful area to explore at this point?

A. his attention span
B. his criminal record
C. his relationship with his mother
D. history of cruelty to animals
E. history of enuresis

Correct Answer: A
Section: Behavioral Science and Biostatics
Explanation

Explanation/Reference:
Explanation:
Acommon cause of disruptiveness is attention deficit hyperactivity disorder (ADHD), which is characterized by inattention and hyperactivity. Enuresis (choice E), cruelty to animals (choice D), and trouble with the law (choice B) are often found in the childhoods of those who are eventually diagnosed as having an antisocial personality, but disruptiveness in class is more indicative of hyperactivity. Exploring Sean's relationship to his mother (choice C) may be useful, but not as much as assessing his attention span.

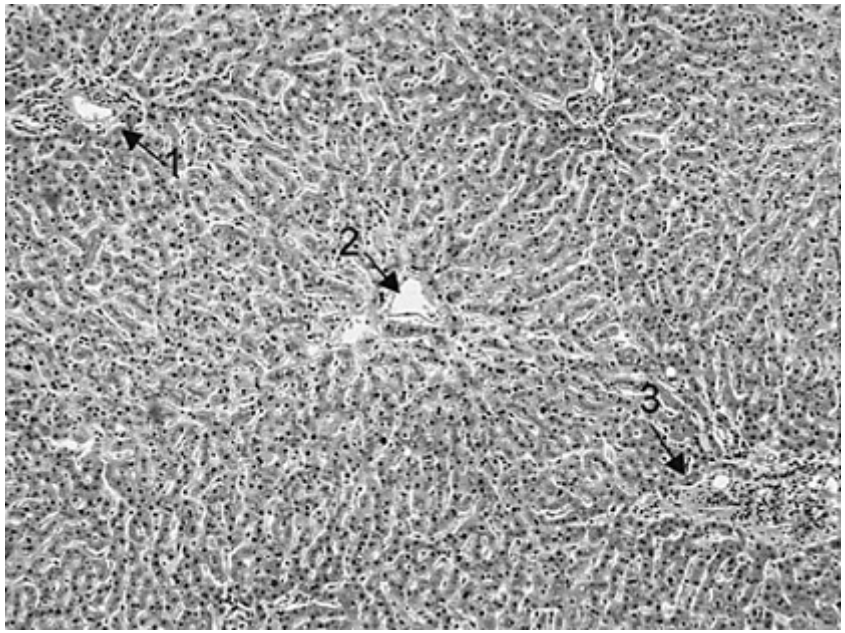
QUESTION 670
Thomas is a 9-year-old child of normal physical stature and health. He is unruly at school and refuses to abide by instructions given to him by his teachers. In addition, he has had inattention, hyperactivity, and impulsivity since the age of 5. Which of the following is the most likely diagnosis?

A. anaclitic depression
B. attention deficit hyperactivity disorder
C. conduct disorder
D. generalized anxiety disorder
E. separation anxiety disorder

Correct Answer: B
Section: Behavioral Science and Biostatics
Explanation

Explanation/Reference:
Explanation:
The diagnostic criteria for ADHD include inattention, hyperactivity, and impulsivity invarious areas, and the symptoms must have been present before the age of 7. The specific history of inattention and hyperactivity tend to rule out choices A, C, D, and E, although there may be some elements of conduct disorder.

QUESTION 671
In following figure, arrow 2 points to which of the following specific structures



A. central vein
B. hepatic lobule
C. portal tract
D. sinusoid
E. Space of Disse

Correct Answer: A
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
Arrow 2 points to the central vein which defines the center of each hepatic lobule (choice B). Arrows 1 and 3 point to portal tracts (choice C), which are located at the angles of the margins of the hepatic lobule. The sinusoids (choice D) originate from the margins of the lobules and converge to the central vein by running between the plates of hepatocytes. The space of Disse (choice E) is found between the sinusoid lining cells and the surfaces of the hepatocytes. It is best seen in electron micrographs and not in a photomicrograph.

QUESTION 672
Alarge vascular infarct involving the posterior limb of the internal capsule on the right side is likely to produce which of the following deficits?

A. deviation of the protruded tongue to the right
B. hypertonia and hyperreflexia in the right upper limb
C. paralysis of facial expression muscles on the lower left portion of face
D. paraplegia involving the lower extremities
E. spastic hemiplegia involving the right side of the body

Correct Answer: C
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
Capsular lesions of the corticobulbar system produce the “central seven” symptoms. Loss of the descending cortical fibers to the contralateral facial nucleus (cranial nerve VII) primarily affects the muscles of facial expression in the lower portion of the face, particularly those around the angle of the mouth and the nasolabial fold. Deviation of the protruded tongue (choice A), hypertonia/hyperreflexia (choice B), and spastic hemiplegia (choice E) are symptoms that result from a capsular lesion, but they would be seen contralateral to the affected capsule, and in this case would involve the left side of the body. Paraplegia (choice D) is not typically seen following a unilateral capsular lesion.

QUESTION 673
An 8-year-old boy is referred to a neurologist by his family physician because he has developed progressive slow and clumsy walking. On examination, the patient has difficulty with standing and running. While standing, he adopts a wide-based gait with constant shifting of position to maintain his balance. Sitting or standing, he also displays a constant tremor of the head and trunk. When asked to walk, his feet strike the ground in an uneven and irregular rhythm; if he attempts to correct his imbalance, he displays wild and abrupt movements. A magnetic resonance image (MRI) reveals demyelination in the dorsal columns, corticospinal and spinocerebellar tracts. The child is diagnosed with Friedreich's ataxia, an autosomal recessive neurological disorder resulting from mutation of a gene locus on chromosome 9. Second-order neurons of the dorsal (posterior) spinocerebellar tracts are located in which of the following?

A. deep cerebellar nuclei
B. dorsal root ganglion
C. nucleus cuneatus
D. nucleus dorsalis (Clarke's column)
E. Rexed's lamina IX of the spinal cord

Correct Answer: D
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The nucleus dorsalis (Clarke's column, Rexed's lamina VII of the spinal cord) contains the cell bodies of the second order neurons of the dorsal (posterior) spinocerebellar tract. Axons from these neurons ascend ipsilaterally in the lateral funiculus of the spinal cord, join the restiform body of the inferior cerebellar peduncle, and terminate in the vermis of the cerebellum as mossy fibers. The dorsal (posterior) spinocerebellar tract conveys proprioception from muscle spindles and Golgi tendon organs. Collateral branches of this tract also terminate in the deep cerebellar nuclei (choice A). The dorsal root ganglion (choice B) contains the cell bodies of sensory neurons, including the first-order neurons of the dorsal (posterior) spinocerebellar tract. The nucleus cuneatus (choice C) contains the second order neurons of the dorsal column pathways, responsible for conveying sensations of fine touch, pressure, and vibration sense. Rexed's lamina IX of the spinal cord (choice E) contains the spinal cord motorneurons responsible for the innervations of voluntary muscles.

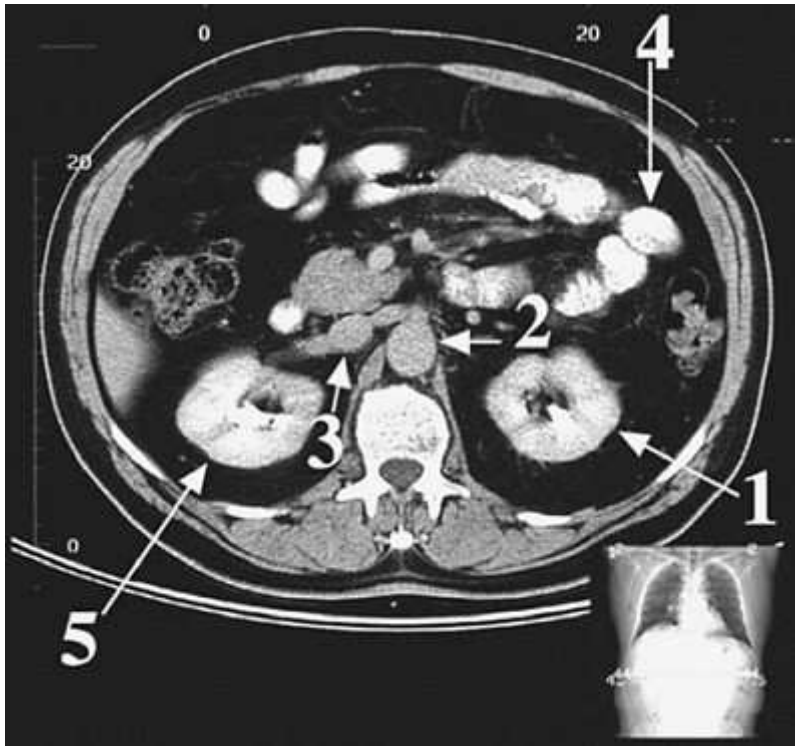
QUESTION 674
An 8-year-old male patient is brought to a rural hospital with a history of recurrent infection. The patient has a characteristic facies with a high, broad nasal bridge, long face, narrow palpebral fissures, and an abnormally small mandible. The patient also has a cleft palate. The patient is diagnosed with DiGeorge syndrome, an inherited immunodeficiency disease due to a chromosome 22q11.2 deletion. In this syndrome, the production of which of the following cells is affected in the thymus?

A. B cells
B. endothelial cells
C. macrophages
D. neutrophils
E. T cells

Correct Answer: E
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
In DiGeorge syndrome, the cortical epithelial cells of the thymus fail to develop and the thymus is hypoplastic. As a result, bone marrow-derived T-cell precursors cannot differentiate and functional T- cell production is markedly reduced. The development of B cells (choice A) is not affected in DiGeorge syndrome. Endothelial cells (choice B) forming the vascular walls are not affected by thymic maldevelopment, nor are the cells of myeloid lineage, the macrophages (choice C), and the neutrophils (choice D).

QUESTION 675
A third-year medical student is asked to review the computerized tomographic (CT) results of a patient with a possible abdominal aortic aneurysm. Which of the following arrows in Following figure points to the abdominal aorta?

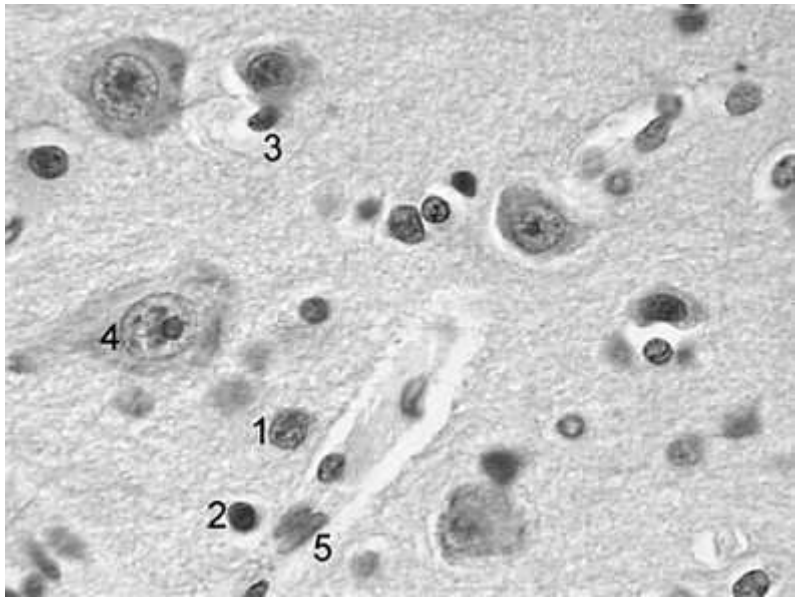


A. 1
B. 2
C. 3
D. 4
E. 5

Correct Answer: B
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
Arrow 2 points to the abdominal aorta, located anterior to the lumbar vertebra. Arrows 1 (choice A) and 5 (choice B) indicate the left and right kidneys respectively. Arrow 3 points to the inferior vena cava; the junctions of the left and right renal veins to the inferior vena cava are seen in this CT scan. Arrow 4 points to a loop of the small intestine, filled with contrast-enhancing material.

QUESTION 676
A young resident doing a fellowship in neuropathology is asked to review histological slides from the cerebral cortex of a 79-year-old nursing home resident, who died of multiinfarct dementia. The resident is asked to estimate the density of neurons in the infracted brain area. To prepare himself for the task, he first reviews slides from the normal areas of the cerebral cortex. Referring to following figure,which of the following structures does he correctly identify as neurons?



A. 1
B. 2
C. 3
D. 4
E. 5

Correct Answer: D
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
Routine neuropathological identification of cells in the central nervous system is based on nuclear morphology using a stain such as the hematoxylin-eosin (H&E) stain shown in Fig. 1-10. The largest nuclei belong to neurons. Nuclei of glial cells are smaller and decrease in size from astroglia (choice A), to oligodendroglia

(choice B), to microglia (choice C). Endothelial cells of the penetrating vasculature of the brain represent choice E.

QUESTION 677
A professional football player was diving for a touchdown when his face mask was grabbed and wrenched, causing neck hyperextension and rotation to the right. When brought to the sideline, the player complained of a burning sensation radiating down the right upper extremity and neurological examination revealed right lateral weakness of this limb. Movements affected were arm rotation and flexion, elbow flexion, forearm supination, and thumb flexion. The patient is diagnosed with a brachial plexus injury at the level of C6. 29. Which of the following muscles can perform arm and elbow flexion along with forearm supination?

Which of the following innervates the muscle identified in question 29?

A. median
B. musculocutaneous
C. radial
D. suprascapular
E. ulnar

Correct Answer: B
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The musculocutaneous nerve innervates the biceps brachii along with the coracobrachialis and the brachialis. It continues into the forearm as the lateral antebrachial cutaneous nerve. In this brachial plexus injury, the sudden hyperextension and right rotation of the neck narrow the intervertebral foramina through which exit the cervical nerves. Injury at the level of C6 will affect the musculocutaneous nerve along with the suprascapular nerve, resulting in impairment of the movements described. The median nerve (choice A) and ulnar nerve (choice E) innervate muscles not in the arm but in the forearm and hand. In the arm, the radial nerve (choice C) is the nerve to the only muscle in the extensor compartment, the triceps brachii. The suprascapular nerve (choice D) innervates two muscles of the rotator cuff, the supraspinatus and infraspinatus. It is affected in a brachial plexus injury at the C6 level.

QUESTION 678
A 64-year-old male patient suffering from diabetes has developed a cataract in the left eye. Which of the following is the most likely location of a cataract?

A. lens anterior epithelium
B. lens capsule
C. substance
D. posterior chamber
E. vitreous cavity

Correct Answer: C

Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
A cataract is an opacification of the lens caused by a change in the solubility of the lens proteins filensin and crystallins (, , and). These proteins are synthesized by the cortical lens fibers in the lens substance. Their change in solubility and aggregation result in increased light scattering, forming the cataract, which can only occur in the lens substance. The lens anterior epithelium (choice A) consists of a simple cuboidal epithelium. When these cells reach the equatorial region of the lens, they differentiate into the cortical lens fibers, which then synthesize filensin and the crystallins. The lens capsule (choice B) is a thick and transparent membrane enclosing the lens. The posterior chamber (choice D), located anterior to the lens, and the vitreous cavity (choice E), located posterior to the lens, are not involved in cataract formation.

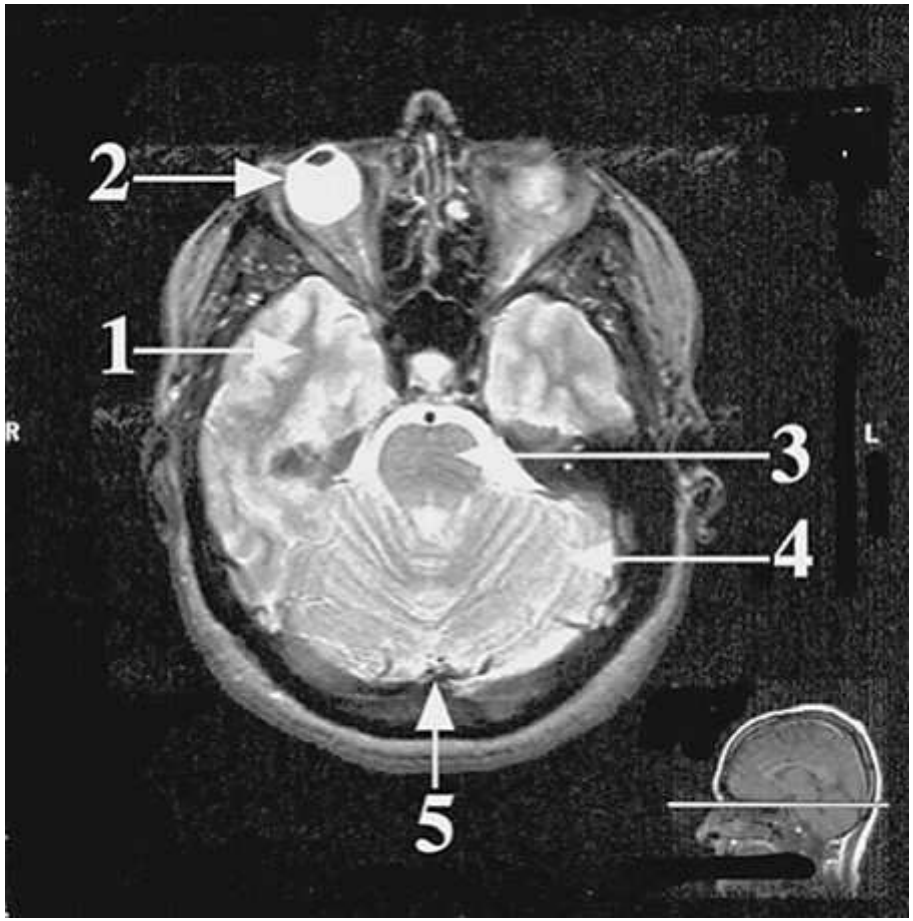
QUESTION 679
During the first 57 days of life, the umbilical vein can be catherized and used for central venous pressure monitoring. The umbilical vein leads to which of the following vessels?

A. descending aorta
B. ductus arteriosus
C. ductus venosus
D. inferior vena cava
E. portal vein

Correct Answer: C
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
In the fetus, the umbilical vein connects directly to the ductus venosus, a fetal vessel which bypasses the liver to bring oxygenated blood to the inferior vena cava (choice D). The descending aorta (choice A) distributes blood to the body and, in the fetal circulation, brings blood to the umbilical arteries by way of the iliac arteries for return to the placenta for oxygenation. The ductus arteriosus (choice B) is a fetal vessel which allows bypass of the oxygenated blood from the pulmonary trunk to the arch of the aorta. The portal vein (choice E) is formed by the union of the splenic vein and the superior mesenteric vein; it returns blood from the digestive system to the liver.

QUESTION 680
A 30-year-old patient displays ataxia of extremities and asynergy with decomposition of movement. He also has dysmetria (past-pointing phenomenon), dysdiadochokinesia (the inability to perform rapidly alternating movements), and intention tremor. These neurological signs are characteristic of a lesion in the structure indicated by which arrow in following figure ?



A. 1
B. 2
C. 3
D. 4
E. 5

Correct Answer: D
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The collective neurological signs are characteristic of a lesion of the neocerebellum (cerebellar hemispheres). Alesion in the archicerebellum (cerebellar vermis; arrow 5, choice E) results in loss of equilibrium. None of the other choices apply to the collection of neurological signs displayed by this patient: arrow 1 (choice A) points to the temporal lobe, arrow 2 (choice B) to the eyeball, and arrow 3 (choice C) to the pons.

QUESTION 681
Which structure most effectively prevents toxic molecules from penetrating an epithelium by passing between adjacent epithelial cells?

A. desmosome
B. gap junction
C. hemidesmosome
D. terminal bar
E. tight junction

Correct Answer: E
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The space between plasmalemmas of adjacent epithelial cells is obliterated at the tight junction (zonula occludens), which forms by fusion of the membranes along narrow anastomosing bands. The tight junction is the apical--most part of the junctional complex, which is typical of epithelia lining tubular and hollow organs. The zonula adherens and desmosome (choice A) also contribute to the junctional complex, but they hold adjacent cells together. The gap junction (choice B) functions to electrically and chemically couple adjacent cells. It consists of direct channels (connexons) between cells, but there is a significant space (about 2 nm) separating the membranes between the channels. The hemidesmosome (choice C) is a specialization for adhesion of a cell to its basement membrane. The terminal bar (choice D) is not a type of junction, but rather a manifestation of the junctional complex seen with the light microscope.

QUESTION 682
A 57-year-old female patient has suffered a major stroke and as a result is in a coma. The attending neurologist is very concerned because the patient is developing ataxic breathing. The pneumotaxic center and apneustic centers of the brain are located in which of the following?

A. diencephalon
B. midbrain
C. pons
D. spinal cord
E. telencephalon

Correct Answer: C
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The pneumotaxic center is located in the upper one-third of the pons, whereas the apneustic center is in the lower two-thirds. The apneustic center promotes inspiration and the pneumotaxic center, expiration. The telencephalon (choice E), diencephalon (choice A), midbrain (choice B), and spinal cord (choice D) are not known to contain pneumotaxic or apneustic centers.

QUESTION 683
Potassium supplementation is often necessary for patients taking large doses of which of the following drugs?

A. amiloride
B. captopril
C. hydrochlorothiazide
D. losartan
E. spironolactone

Correct Answer: C
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Hydrochlorothiazide causes potassium wasting and may lead to hypokalemia requiring dietary potassium supplementation. Potassium wasting is characteristic of diuretics that present more sodium to the collecting tubule, where sodium is conserved in exchange for potassium under the control of aldosterone. Therefore, diuretics that act in the proximal convoluted tubule (carbonic anhydrase inhibitors), ascending limb of the loop of Henle (loop diuretics), and distal convoluted tubule (thiazides) cause potassium wasting and may lead to dangerous hypokalemia. Angiotensin antagonists (because they interfere with aldosterone secretion) and aldosterone inhibitors have the opposite effect. Amiloride (choice A) and spironolactone (choice E) are aldosterone antagonists; captopril (choice B) and losartan (choice D) are angiotensin antagonists. The latter agents cause potassium retention and may cause hyperkalemia, not hypokalemia.

QUESTION 684
Which of the following statements about the leukotrienes LT LT and LT is most correct?

C_{4r}

A. Their biosynthesis is inhibited by aspirin.
B. They are chemotactic agents for polymorphonuclear leukocytes.

C. They are potent bronchoconstrictor substances.
D. They are synthesized and stored in platelet granules.
E. They have few cardiovascular effects.

Correct Answer: C
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
The leukotrienes LT LT and LT are 5'-lipoxygenase metabolites of arachidonic acid. When

$C_{4,}$

lung tissue is challenged with antigen in sensitive individuals, LT is formed and subsequently

$C_{4,}$

metabolized to LT and LT . These leukotrienes are not stored but produce bronchoconstriction,

$C_{4,}$

increased capillary permeability, and increased mucus formation for an extended time because of their slow tissue clearance. Because the first enzyme in synthesis of leukotrienes from arachidonic acid is 5'- lipoxygenase rather than COX, aspirin (choice A) does not inhibit their biosynthesis. Another leukotriene, LT is a potent chemotactic agent for polymorphonuclear leukocytes (choice B), but the

$B_{4,}$

cysteine- inked leukotrienes LT LT , and LT do not share this property. Platelets do not

$C_{4,}$

contain 5'- ipoxygenase (although they do contain 12'-lipoxygenase), and leukotrienes are not stored in platelet granules (choice D). The COX product of arachidonic acid, TX is critical in platelet

$C_{4,}$

physiology, and acetylation of COX by aspirin accounts for the effect of this drug in inhibiting platelet function. The leukotrienes possess significant cardiovascular

effects (choice E); they produce hypotension by decreasing intravascular volume and reducing cardiac contractility by constricting coronary vessels, thus reducing coronary blood flow.

QUESTION 685
The mechanism of action for the therapeutic effect of saquinavir involves which of the following?

A. incorporation into RNA
B. inhibition of thymidylate synthase
C. inhibition of viral DNA polymerase
D. inhibition of viral protease
E. inhibition of viral reverse transcriptase

Correct Answer: D
Section: Pharmacology
Explanation

Explanation/Reference:
Explanation:
Saquinavir is an HIV protease inhibitor. Viral protease cleavage of a polyprotein is necessary for production of the viral coat protein. The HIV protease inhibitors include ritonavir, indinavir, nelfinavir, and amprenavir in addition to saquinavir. Currently available HIV protease inhibitors are not sufficient for monotherapy because of the rapid emergence of resistance due to mutations in the viral protease. Combination therapy using saquinavir with two reverse transcriptase inhibitors such as zidovudine, lamivudine, abacavir, or didanosine is currently effective in reducing viral load. Incorporation into RNA (choice A) is part of the mechanism of action for the antitumor agent 5-fluorouracil (5-FU). Inhibition of thymidylate synthase (choice B) is another part of the mechanism of action for the antitumor agent 5-FU. 5-FU is converted to 5- FdUMP, a potent inhibitor of thymidylate synthase. Inhibition of viral DNA polymerase (choice C) is a mechanism of action for the antiherpesvirus nucleosides acyclovir, valacyclovir, famciclovir, and ganciclovir. These agents are metabolized to their nucleotide triphosphate forms, which competitively inhibit the herpesvirus polymerase. Acyclovir and valacyclovir also cause DNA chain termination. Inhibition of viral reverse transcriptase (choice E) is a property of the nucleosides zidovudine (AZT), didanosine (ddI), lamivudine (3TC), stavudine (d4T), and zalcitabine (ddC). These nucleosides are metabolized to the triphosphate forms that competitively inhibit reverse transcriptase. Nonnucleoside reverse transcriptase inhibitors include nevirapine, delavirdine, and efavirenz. Combinations of agents are used because resistance, through mutations in the reverse transcriptase sequence, frequently arises during monotherapy.

QUESTION 686
A 23-year-old woman complains of depression and anxiety. While describing her symptoms, she looks dazed. A minute later, she looks around the room slowly, and says, in a heavily accented voice with a different tone, "Where am I?" Which of the following does this presentation suggest?

A. adjustment disorder
B. catatonia
C. dissociative identity disorder
D. major depression
E. schizophrenia

Correct Answer: C
Section: Behavioral Science and Biostatics
Explanation

Explanation/Reference:
Explanation:
Dissociative identity disorder (multiple personality disorder) is often associated with memory disturbance and an alternate personality, who may have a different speech tone, accent, or voice. Schizophrenia (choice E) is unlikely; there is no sign of psychosis. Major depression (choice D) is unlikely; there is no sign of depression. Catatonia (choice B) refers to muscle rigidity and mutism, and adjustment disorder (choice A) is a broad diagnostic category that does not include this presentation.

QUESTION 687
Which of the following represents the average age for puberty?

A. 11 for boys and 13 for girls
B. 11 for girls and 13 for boys
C. 14 for boys and 16 for girls
D. 14 for girls and 16 for boys
E. 15 for both girls and boys

Correct Answer: B
Section: Behavioral Science and Biostatics
Explanation

Explanation/Reference:
Explanation:
The onset of puberty varies, but girls usually enter puberty 1218 months earlier than boys. The average age is 11 (range, 813) for girls and 13 (range, 1014) for boys. Choices A, C, and E are incorrect because they do not distinguish between girls and boys. Choice D is above the upper limit for both girls and boys.

QUESTION 688
Which of the following is a normal sexual function?

A. anorgasmia
B. dyspareunia
C. masturbation
D. pedophilia

Correct Answer: C

Section: Behavioral Science and Biostatics
Explanation

Explanation/Reference:
Explanation:
Masturbation is virtually universal among men and women of all cultures. It is common among married as well as single people. Many sex therapists recommend self-stimulation as an auxiliary treatment technique for a variety of sexual dysfunctions. Choices A, B, and D are sexual dysfunctions.

QUESTION 689
Your patient confides in you that she has been losing weight with loss of appetite, has been unable to concentrate, and has had difficulty sleeping through the night. She has also been thinking of the means of killing herself. Which of the following is the most likely diagnosis?

A. borderline personality disorder
B. factitious disorder
C. generalized anxiety disorder
D. hypochondriasis
E. major depression

Correct Answer: E
Section: Behavioral Science and Biostatics
Explanation

Explanation/Reference:
Explanation:
Depression is often accompanied by vague physical symptoms. When a depressed patient presents to a primary physician, it is important that the presence of depression be ascertained by careful history; depressed patients are often suicidal, and about 70% of successful suicides have seen their physician in the previous month. Choices A, B, C, and D are not supported by the signs presented.

QUESTION 690
Robert is 9 years old and has been suspended from school for failing to control his disruptive behavior in the classroom. His parents take him to a psychologist and report that he has been hyperactive and impulsive since the age of 5. Which of the following is the drug of choice for the treatment of this child?

A. buspirone
B. clomipramine
C. dextroamphetamine
D. nefazodone
E. paroxetine

Correct Answer: C

Section: Behavioral Science and Biostatics
Explanation

Explanation/Reference:
Explanation:
Dextroamphetamine and methylphenidate are effective in treating ADHD. Paroxetine (choice E) and nefazodone (choice D) are antidepressants, clomipramine (choice B) is a tricyclic that has special use in obsessive-compulsive disorders, and buspirone (choice A) is an antianxiety agent.

QUESTION 691
Which of the following drugs is useful for the treatment of panic disorder?

A. bupropion
B. olanzapine
C. phenobarbital
D. sertraline
E. valproic acid

Correct Answer: D
Section: Behavioral Science and Biostatics
Explanation

Explanation/Reference:
Explanation:
In addition to SSRIs such as sertraline, paroxetine and fluoxetine, tricyclic antidepressants, MAOIs, and high-potency benzodiazepines such as alprazolam and clonazepam may be effective in panic disorder. Olanzapine (choice B) is an atypical antipsychotic and has not been shown to be effective in panic disorder. Bupropion, an antidepressant (choice A), phenobarbital, a CNS depressant (choice C), and valproic acid, an anticonvulsant and antimanic drug (choice E) are also ineffective in panic disorder.

QUESTION 692
Nancy was tending the goose eggs when they hatched. The young goslings started following Nancy, even when the mother was calling them. Which of the following phenomenon is this an example of?

A. cognitive map
B. imprinting
C. instinctual behavior
D. maternal bonding
E. operant conditioning

Correct Answer: B

Section: Behavioral Science and Biostatics
Explanation

Explanation/Reference:
Explanation:
Imprinting is an ethologic term that indicates a critical period in a newborn animal's life. For example, if goslings are exposed to humans rather than geese shortly after hatching, they will follow humans rather than their own mother.

QUESTION 693
A 58-year-old male visits your office and complains about impotence. Upon questioning you learn that he is capable of erections, but that they do not last as long and that they are of lesser strength than the previous ones. Which of the following neurotransmitters is primarily responsible for dilation of the penile artery during erections?

A. acetylcholine
B. epinephrine
C. GABA
D. nitric oxide
E. norepinephrine

Correct Answer: D
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
Nitric oxide has important neurotransmitterlike functions. Its short half-life, due to spontaneous decay, limits its range and action. Nitric oxide acts on smooth muscle cells in a generally inhibitory manner; it relaxes the GI muscles and sphincters and dilates blood vessels. In blood vessels, nitric oxide is derived from endothelial cells and has been identified as the long-hypothesized endothelium-derived relaxing factor (EDRF). Acetylcholine (choice A) is the classic neurotransmitter of the parasympathetic nervous system. Although activation of the pelvic parasympathetic nerves leads to erection, it is nitric oxide and not acetylcholine that relaxes penile artery smooth muscle cells. GABA (choice C) is an inhibitory neurotransmitter found in the central nervous system. Epinephrine (choice B) and norepinephrine (choice E) play a role during the ejaculation phase of the male sexual act, but do not contribute to penile artery dilation during the erectile phase.

QUESTION 694
Exhibit:

A. N-type calcium channels
B. Na^+ : Ca^{2+} exchange protein (NCX)
C. plasma membrane calcium ATPase (PMCA)
D. potassium channels
E. sodium channels

Please refer to the exhibit.
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. A
B. B
C. C
D. D
E. E

Correct Answer: B
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
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 [C]. However, PMCA activity is not directly involved in the mechanism of

a^{2+}

action of digoxin.

QUESTION 695
A 68-year-old postmenopausal female with a history of osteoprosis and essential hypertension is placed on the thiazide diuretic chlorothiazide, which has a beneficial action toward both conditions. Which letter in below figure depicts the tubular location of epithelial cells containing a / cotransport

Na^+

protein inhibited by thiazide diuretics?

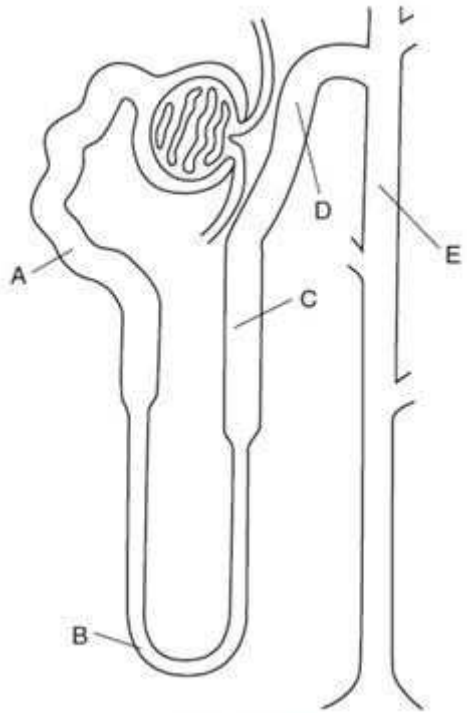


FIG. 2-25

A. A
B. B
C. C
D. D
E. E

Correct Answer: D
Section: Physiology

Explanation

Explanation/Reference:
Explanation:
The epithelial cells of the early portion of the distal tubule contain a / cotransporter that is

Na^+

inhibited by thiazide diuretics which promote a diuresis and a natriuresis, and which secondarily, promote increased renal reabsorption of filtered calcium. Choices A and B denote the proximal and thin loop of Henle segments, respectively; which do not have the properties of the early distal tubular segment. Likewise, choices C and E denote the thick ascending loop of Henle and the collecting duct, which also do not have the same properties as the early distal tubular segment.

QUESTION 696
Worldwide, one of the most common parasitic infections is schistosomiasis. Assume a complete blood cell count is performed in a patient with this condition. Which of the following blood cells would most likely be present in elevated amounts?

A. eosinophils
B. erythrocytes
C. monocytes
D. neutrophils
E. platelets

Correct Answer: A
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
Eosinophils normally constitute about 2% of all blood leukocytes. These cells are phagocytic and exhibit chemotaxis. Their primary role is in fighting parasitic infection. In schistosomiasis the eosinophil attaches to the immature parasite and, by releasing various cytotoxic compounds, is able to kill the parasite. Erythrocytes (choice B) are the most numerous blood cells. They are not leukocytes, but function in blood gas transport. Erythrocyte number would not be increased in schistosomiasis. Monocytes (choice C) are leukocytes found in the blood. They are immature cells which migrate to the tissues, where they mature into macrophages. These cells are very active in phagocytosis and play a prominent role in the inflammatory response. They are not, however, particularly important in parasitic infections. Neutrophils (choice D) are another type of leukocyte that, though essential to combat bacterial infections, are not particularly sensitive to parasitic challenge. Platelets (choice E) are not leukocytes. The platelet is a cell fragment that functions in hemostasis.

QUESTION 697
The patient is a 43-year-old male. He is anemic, with a hemoglobin level of 12.2 g/dL (normal is 15.5 g/dL). The erythrocytes are microcytic (MCV = 70 fL, with normal MCV = 80100 fL). Which of the following would most likely be present in this patient?

A. acute bleeding
B. folate deficiency
C. iron deficiency
D. vitamin deficiency
E. vitamin K deficiency

Correct Answer: C
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
Microcytic anemia can often be associated with defective hemoglobin synthesis. In the case of iron deficiency, heme synthesis is impaired due to the lack of iron. Acute bleeding (choice A) is normally associated with erythrocytes of normal size, since the anemia is due to simple loss of blood, with plasma expansion to maintain total volume. Both vitamin and folate (choices B and D) are

B_{12}

required for DNA synthesis. Due to the extremely active cell division required to sustain the erythrocyte pool, impaired DNA synthesis first normally manifests as a lack of erythrocyte production. Anemia due to vitamin B12 or folate deficiency is macrocytic. Vitamin K (choice E) is required for synthesis of several clotting factors. Lack of vitamin K often presents as a problem with coagulation.

QUESTION 698
Which of the following statements concerning total body energy storage is correct?

A. Most of the body's energy store is held as carbohydrate.
B. Most of the body's energy store is held as lipid.
C. Most of the body's energy store is held as plasma glucose.
D. Most of the body's energy store is held as protein.
E. Total body's energy storage approximately equals resting metabolic rate.

Correct Answer: B
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
Lipid is the most concentrated form of energy storage, holding 9.4 kcal/g. For a typical 70 kg human over 130,000 kcal is typically stored as fat. Storage of energy as available protein (choice D) is about 20,000 kcal, while storage as carbohydrate (choice A) is about 3,000 kcal. Though blood glucose (choice C) is critically

important, in particular as a source of energy for the brain, blood glucose does not provide a significant fraction of total body energy storage. While total body energy stores typically exceed 150,000 kcal, resting metabolic rate (depending on age and body mass) is about 2100 kcal/day (choice E).

QUESTION 699
During a brain surgery, during which the patient remained conscious, a part of the DC/ML (dorsal column, medial lemniscal) system was exposed and stimulated. Which of the following sensations might the patient most likely experience?

A. a feeling as if his fingers are warming up
B. a feeling as if something were touching his index finger
C. a tingling sensation
D. mild pain but he is unable to explain exactly where it hurts

Correct Answer: B
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
The dorsal column-medial lemniscus (DC/ML) system is the sensory pathway that transmits conscious proprioceptive information with fine gradations such as a fine touch on the index finger to the cerebral cortex. The brain interprets any signals coming along the "labeled lines," the nerves that carry messages from the sensory organ to the cortex, as being information about a particular sense. Hence, activation of certain neurons in the somatic sensory system can cause a sensation as if it originated from mechanical pressure on the finger (choice E). Thermal sensations (choice A), tingling (choice C), and crude undetermined pain (choice D) are sensory modalities that are processed in the spinothalamic or anterolateral system.

QUESTION 700
A 2-year-old male patient develops progressive generalized weakness and muscle atrophy. The impairment first began with the muscles of the hips, and then progressed to the pelvic area, thigh, and shoulder muscles. The patient is diagnosed with Duchenne's muscular dystrophy, a congenital disorder where the protein dystrophin is deficient. Which of the following describes the role of dystrophin in muscle tissue?

A. anchors actin to the sarcolemma
B. endows the myosin filaments with elastic recoil properties
C. extends from Z disk to Zdisk, forming a supportive network
D. inhibits the binding of myosin to actin
E. protects desmin filaments from stressinduced damage

Correct Answer: A
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
Dystrophin anchors actin to the sarcolemma, reinforcing and stabilizing the latter during muscle contraction. Titin is a large protein which associates with myosin filaments and endows them with elastic recoil properties (choice B). Desmin filaments form a supportive network extending from Z disk to Zdisk (choice C). Troponin I inhibits the binding of myosin to actin (choice D). AlphaB-crystallin protects desmin filaments from stress-induced damage (choice E).

QUESTION 701
The third week of development is characterized by the appearance of the branchial apparatus, the embryonic primordium from which head and neck structures will be derived. The apparatus consists of five branchial arches, numbered 1, 2, 3, 4 and 6. Second arch anomalies represent 95% of all branchial anomalies and are classified into four types with types IIII being the most common. The anomalies manifest as cysts or fistulae in the lateral neck, located anterior and deep to the sternocleidomastoid muscle. Which of the following structures develop from the second branchial arch?

A. anterior digastric muscle
B. posterior cricoarytenoideus muscle
C. posterior digastric muscle
D. stylopharyngeus muscle
E. superior constrictor muscle

Correct Answer: C
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The posterior digastric muscle is derived from the second branchial arch and thus is innervated by its nerve, the facial (Seventh cranial) nerve. The anterior digastric muscle (choice A) is derived from the first branchial arch and is innervated by its nerve, the mandibular division of the trigeminal (fifth cranial) nerve. The posterior cricoarytenoideus muscle (choice B) and the superior constrictor muscle (choice E), derived from a combination of the fourth and sixth branchial arches, are innervated by the vagus (tenth cranial) nerve. The stylopharyngeus (choice D) is derived from the third branchial arch and is the only voluntary muscle innervated by the glossopharyngeal (ninth cranial) nerve.

QUESTION 702
A 10-year boy is examined because his parents noticed that "his eyes never seem to look in the right direction." On examination, the left eye of the child is unable to move laterally (abduction) and when asked to look toward the nose (adduction), the eyeball retracts into the socket and the eye opening narrows. Sometimes, the eye also moves superiorly. The child is diagnosed with Duane syndrome, a congenital ocular motility disorder characterized by limited abduction of the affected eye. This is due to absence of the abducens (fifth cranial) nerve with aberrant innervation by the oculomotor (third cranial) nerve. Which of the following muscles is normally innervated by the abducens nerve?

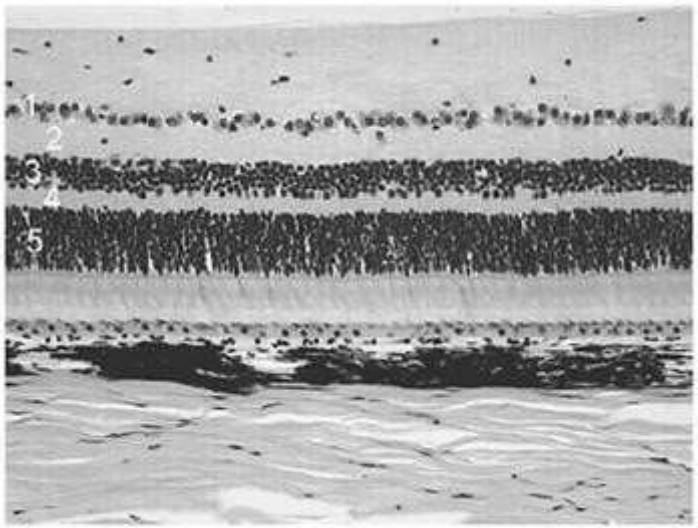
A. inferior oblique
B. lateral rectus
C. medial rectus

D. superior oblique
E. superior rectus

Correct Answer: B
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The abducens (sixth cranial) nerve normally innervates the lateral rectus muscle. The inferior oblique (choice A), medial rectus (choice C), and superior rectus (choice E) are all innervated by the oculomotor (third cranial) nerve. The superior oblique (choice D) is innervated by the trochlear (fourth cranial) nerve. In Duane syndrome, the absence of lateral rectus innervations by the abducens (sixth cranial) nerve is replaced by an aberrant innervation of the oculomotor (third cranial) nerve. Thus when the patient is asked to adduct the affected eye, there is cocontraction of the lateral and medial recti with globe retraction.

QUESTION 703
Retinitis pigmentosa is a hereditary disorder, which affects the photoreceptors (the rods and the cones) in the retina. These photoreceptors are located in which of the numbered layers in Figure below



A. 1
B. 2
C. 3

D. 4
E. 5

Correct Answer: E
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The retina contains three layers of cells. They are, from top to bottom, the ganglion cells (choice A), the bipolar cells (choice C), and the photoreceptor cells (rods and cones, choice E). The internal plexiform layer (choice B) contains the synapses between the bipolar cells and the ganglion cells. The external plexiform layer (choice D) contains the synapses between the photoreceptors and the bipolar cells. Remember that light enters from the top and traverses all the layers to reach the photoreceptors in the bottom layer.

QUESTION 704
In a medial medullary syndrome that involves a left-sided branch of the anterior spinal artery, which of the following deficits is seen?

A. deviation of the tongue to the left, hemiplegia of arm and leg on the left
B. deviation of the tongue to the right, hemiplegia of arm and leg on the right
C. loss of conscious proprioception and precise tactile discrimination over the right side of the body exclusive of the face
D. only deviation of the tongue to the left
E. only hemiplegia on the right

Correct Answer: C
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
A vascular lesion affecting the left caudal medulla involves the left medial lemniscus, left hypoglossal nerve fibers, and the left medullary pyramid. Involvement of the left medial lemniscus produces somatosensory deficits involving the right side of the body. Damage to the left hypoglossal nerve would result in deviation of the protruded tongue to the left (and other lower motoneuron signs), and damage to the left pyramid results in right hemiplegia (choices A and B involve incorrect combinations) along with other upper motoneuron signs. Choices D and E are incorrect because they fail to combine involvement of the tongue and contralateral hemiplegia.

QUESTION 705
A neurologist is performing the neurological examination on a patient who recently suffered a head trauma. You note that, as part of the examination, she uses a cotton swab to touch the upper part of the auricle, the external auditory meatus, and the lobule. The external auditory meatus of the ear is innervated by which of the following?

A. vagus (tenth cranial) nerve
B. great auricular nerve
C. auriculotemporal nerve
D. greater occipital nerve
E. facial (seventh cranial) nerve

Correct Answer: A
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The vagus (tenth cranial) nerve innervates the external auditory meatus of the ear. The great auricular nerve (choice B) innervates the lobule of the auricle and the auriculotemporal nerve (choice C), the superior aspect of the auricle. In fact, a sensory test which includes these three parts of the ear tests the integrity of the trigeminal (fifth cranial) nerve by the auriculotemporal nerve, the vagus (tenth cranial) nerve by its branch innervating the auditory meatus, and spinal nerves C2-3 by their great auricular branch. The test thus covers the upper and lower medulla and the upper spinal cord. The greater occipital nerve (choice D) is a branch of the cervical plexus originating from C2 and innervates the scalp of the back of the head. The facial (seventh cranial) nerve provides only motor innervation to the face and scalp areas.

QUESTION 706
A 48-year-old male patients is brought to the emergency room because of intense pain of the right face and neck with transient visual loss of the right eye. On examination, the patient has palsy of the oculomotor nerve on the right side with resulting diplopia, along with a right lateralized painful Horner syndrome. This constellation of signs is suggestive of a cervical carotid dissection, which is a separation of the arterial tunical intima from the subjacent tunica media. Which numbered structure in following figure, is the tunica intima?

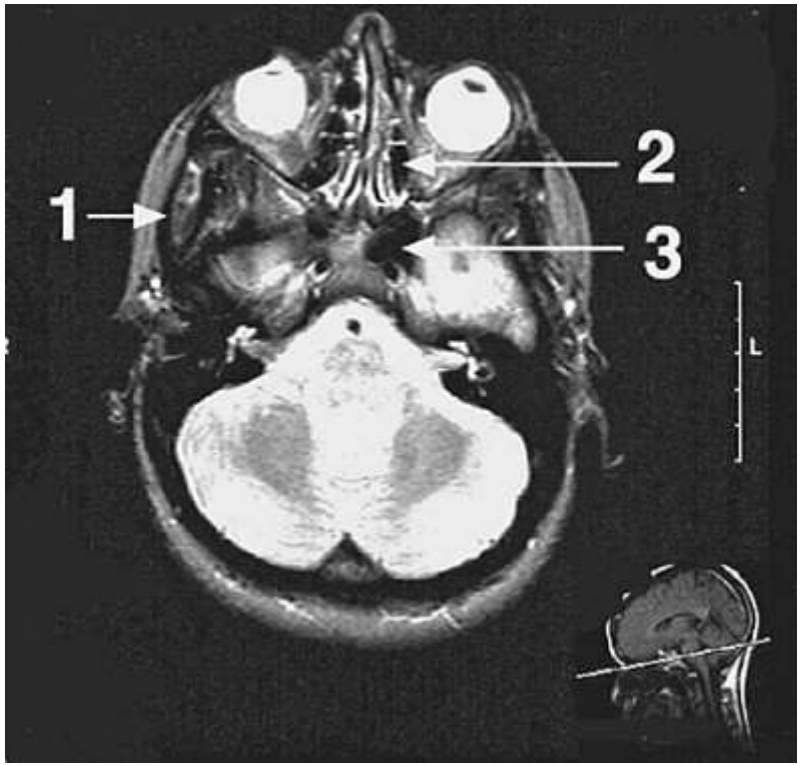
A. 1
B. 2
C. 3
D. 4
E. 5

Correct Answer: D
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
Arrow 3 points to the tunica intima. The carotid artery is an elastic artery, which contains the following layers aside from the tunica intima: Tunica externa (arrow 1), and tunica media (arrow 5). In a carotid dissection, the tunica intima can elevate or separate from the tunica media with accompanying hemorrhage of the arterial

wall. The most common clinical signs are ophthalmological manifestations including painful Horner syndrome, palsy of the oculomotor nerve, diplopia, and transient monocular visual loss. Arrow 2 points to a vasa vasorum, vessels which nourish the thick wall of the aorta. Arrow 4 points to the adipose tissue in the tunica externa.

QUESTION 707
The structure indicated by arrow 2 in following figure, is which of the following?



A. ethmoidal sinus
B. inferior nasal meatus
C. infratemporal fossa
D. maxillary sinus
E. sphenoidal sinus

Correct Answer: A

Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
This axial scan is at the level of the orbits as indicated by the insert at the bottom right and the eyeballs in the orbits. Arrow 2 points to the ethmoidal sinus located medial to the orbits. The sinus is divided into compartments by the air cells. The maxillary sinus (choice D) and the inferior nasal meatus (choice B) are located inferior to the level of this scan and are not seen. The sphenoidal sinus (choice E) is indicated by arrow 3 and the infratemporal fossa (choice C) by arrow 1.

QUESTION 708
A stroke resulting from obstruction of the structure indicated by arrow 1 in following figure, may result in ischemia in which of the following brain regions?

A. Broca's area in the left frontal lobe
B. cerebellum
C. medial aspect of the right frontal lobe
D. pons
E. Wernicke's area in the left frontal lobe

Correct Answer: C
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
Arrow 1 points to the right internal carotid artery which supplies the anterior and middle cerebral arteries in the brain. The territory of the right anterior cerebral artery includes the rightmedial aspect of the frontal lobe, which will be affected by obstruction of the internal carotid artery. Broca's (choice A) and Wernicke's (choice E) areas are located in the majority of the population in the left cerebral hemisphere and are supplied by the left middle cerebral artery from the left internal carotid artery. They will not be affected in this case. The cerebellum (choice B) and pons (choice D) receive their blood supply from the basilar artery (arrow 2) which is formed from the vertebral arteries.

QUESTION 709
In the brain, the amygdala plays an important role in emotional processing. Patients with lesion of the amygdala display impairment in enhanced perception of emotionally salient events. Which of the following is a major output pathway from the amygdala?

A. fasciculus arcuatus
B. fasciculus cuneatus
C. fasciculus of Vicq d'Azyr
D. fornix
E. stria terminalis

Correct Answer: E
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The stria terminalis or fasciculus of Foville is one of the major output pathways from the amygdala to the septal, hypothalamic, and thalamic nuclei. Another main amygdaloid output pathway is the ventral amygdalofugal pathway. The fasciculus arcuatus (choice A) or superior longitudinal fasciculus is a bundle of fibers in the cerebrum connecting ipsilateral regions of the frontal, temporal, parietal, and occipital lobes. The fasciculus cuneatus (choice B) carries ascending sensory fibers in the dorsal funiculus of the spinal cord and terminates in the nucleus cuneatus of the medulla oblongata. The fasciculus of Vicq d'Azyr (choice C) or mammillothalamic tract connects the mammillary bodies to the anterior nuclei of the thalamus. This bundle of fibers forms part of Papez circuit, which is also involved in emotional processing. Another part of Papez circuit is the fornix (choice D), a large efferent pathway from the hippocampus.

QUESTION 710
An infant is born anencephalic. He presents without both a forebrain and a cerebrum. The remaining brain tissue is exposed, not covered by bone or skin. The infant is blind, deaf, unconscious, and unable to feel pain. Because the infant has a rudimentary brainstem, reflex actions such as respiration (breathing) and responses to sound or touch occur. However, the lack of a functioning cerebrum permanently rules out the possibility of ever gaining consciousness. Anencephaly is the result of a defect in which of the following?

A. closure of the caudal neuropore
B. closure of the rostral neuropore
C. formation of the first branchial arch
D. formation of the somites
E. fusion of the metopon

Correct Answer: B
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
Malclosure of the rostral neuropore during the fourth week of development results in anencephaly and is lethal in the affected newborn. The condition is better termed meroanencephaly because of the presence of the rudimentary brainstem with some functioning nervous tissues. Defects in the closure of the caudal neuropore (choice A) result in varying conditions of spina bifida at the lower end of the spinal cord. The first branchial arch (choice C) and the somites (choice D) do not play any role in the formation of the brain. Fusion of the metopon or forehead (choice E) occurs after birth and also does not play a role in brain formation.

QUESTION 711
As the consulting physician to the US Open, you are asked to examine a golfer who complains of increased pain with right wrist flexion and pronation activities. The patient also reports discomfort even when simply shaking hands with someone. Examination reveals also decreased sensation in the territory of the ulnar nerve. Your diagnosis is golfer's elbow, affecting mostly the superficial flexor muscles of the forearm. This group of muscles has a common origin from which of the

following bony landmarks?

A. head of the radius
B. lateral epicondyle of the humerus
C. medial epicondyle of the humerus
D. olecranon process of the ulna
E. tuberosity of the radius

Correct Answer: C
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The superficial layer of flexor muscles of the forearm all originate from the medial epicondyle of the humerus. Thus, this condition is also called medial epicondylitis and the most common finding is tenderness with palpation over the anterior aspect of the medial epicondyle. The muscles involved are most often the Pronator Teres, Flexor Carpi Radialis, and Palmaris Longus. The Flexor Digitorum Superficialis and Flexor Carpi Ulnaris may also be affected. There is no muscle attachment to the head of the radius (choice A). The lateral epicondyle of the humerus (choice B) is the attachment point of the common extensor tendon. The olecranon process of the ulna (choice D) is the attachment point for the Triceps Brachii, Flexor Carpi Ulnaris, and Anconeus. The tuberosity of the radius (choice E) receives the distal tendon of the biceps brachii.

QUESTION 712
A professional football player was diving for a touchdown when his face mask was grabbed and wrenched, causing neck hyperextension and rotation to the right. When brought to the sideline, the player complained of a burning sensation radiating down the right upper extremity and neurological examination revealed right lateral weakness of this limb. Movements affected were arm rotation and flexion, elbow flexion, forearm supination, and thumb flexion. The patient is diagnosed with a brachial plexus injury at the level of C6. 29. Which of the following muscles can perform arm and elbow flexion along with forearm supination?

A. biceps brachii
B. brachialis
C. brachioradialis
D. coracobrachialis
E. supinator

Correct Answer: A
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:

The biceps brachii muscle attaches proximally by its short head to the coracoid process of the scapula and by its long head to the supraglenoid tubercle. Distally it attaches by a strong tendon to the tuberosity of the radius and by an aponeurosis to the ulna. It thus can perform arm and elbow flexion along with forearm supination. The brachialis (choice B) attaches proximally to the anterior aspect of the lower half of the humerus and distally to the coronoid process of the ulna. It can only perform elbow flexion. The brachioradialis (choice C) attaches from the lateral supracondylar ridge of the humerus to the base of the styloid process of the radius. Although innervated by the nerve to the extensor compartment, the radial nerve, it performs elbow flexion and forearm pronation. The coracobrachialis (choice D) attaches from the coracoid process of the scapula to the anterior aspect of the upper half of the humerus. It performs arm flexion and weak adduction. The supinator (choice E) attaches proximally to the lateral epicondyle of the humerus and the annular ligament of the radius. Distally, it covers nearly the upper third of the radius and attaches to its lateral anterior aspect. It supinates the forearm, but is a weaker supinator than the biceps brachii.

QUESTION 713
In cleaning the teeth in a patient, a dental hygienist accidentally cuts the gums of the posterior two molar teeth in the lower jaw on the lateral side. The pain of this injury is registered by which of the following nerves?

A. anterior, middle, and posterior superior alveolar nerves
B. buccal nerve
C. greater palatine nerve
D. lingual nerve
E. nasopalatine nerve

Correct Answer: B
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The gums on the lateral side of the mandibular molar teeth are innervated by the buccal nerve (long buccal nerve). All three superior alveolar nerves (choice A) supply the gums lateral to all maxillary teeth. The greater palatine nerve (choice C) innervates the gums medial to the maxillary premolar and molar teeth. The lingual nerve (choice D) supplies the gums medial to all mandibular teeth. The nasopalatine nerve (choice E) innervates the gums posterior to the maxillary incisors.

QUESTION 714
Recanalization of the bile duct after the 13th week after fertilization allows for bile produced in the liver to reach the duodenum. However, if recanalization fails to occur and this cannot be corrected surgically, the affected infant will need a liver transplant. During development, the liver arises from which of the following?

A. foregut
B. hindgut
C. midgut
D. pleuroperitoneal membrane
E. septum transversum

Correct Answer: A
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The liver arises as a ventral outgrowth from the caudal portion of the foregut. The midgut (choice C) arises past the junction point between the bile duct and the duodenum, distal to the formative outgrowth of the liver. The midgut gives rise to the small intestine and part of the large intestine. The hindgut (choice B) arises further distally and gives rise to the rest of the large intestine, the superior part of the anal canal, the epithelium of the urinary bladder, and most of the urethra. The pleuroperitoneal membrane (choice D) and the septum transversum (choice E) are developmental components of the diaphragm.

?

QUESTION 715
A 48-year-old female patient is brought to the emergency room by her husband. He reports that his wife suffers from hypertension but, as a high-level executive with a lot of pressure at work, she has been neglecting to take her medication. This morning, as he entered the garage to leave for work, he found his wife lying on the ground next to her own car. She was experiencing uncontrolled flailing of the left arm and leg. What is the most likely site of brain lesion in this patient?

A. anterior limb of the left internal capsule
B. anterior limb of the right internal capsule
C. cerebellum
D. left subthalamic nucleus of Luys
E. right subthalamic nucleus of Luys

Correct Answer: E
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
Hemiballismus is a movement disorder characterized by involuntary large amplitude movements of one or both limbs on one side of the body. It results from infarct damage to the contralateral subthalamic nucleus of Luys, in this case the right one. The left subthalamic nucleus (choice D) controls the limbs on the right side of the body, which are not affected in this case. The anterior limbs of the internal capsule (choices Aand B) contain mainly thalamocortical and corticothalamic fibers and lesions in these areas do not result in hemiballismus. Lesions in the cerebellum (choice C) also do not result in hemiballismus.

QUESTION 716
During a direct inguinal hernia repair operation, the attending surgeon reminds the firstyear surgical resident that an anatomical variation for the origin of the obturator artery exists. This artery normally arises from the internal iliac artery but it may also originate directly from which of the following vessels?

A. common iliac artery
B. external iliac artery
C. inferior epigastric artery
D. inferior vesical artery
E. superior vesical artery

Correct Answer: C
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The obturator artery can originate from the inferior epigastric artery, a location which renders it vulnerable during inguinal hernia surgical repair. The common iliac artery (choice A) only has two branches, the external and internal iliac arteries. Within the pelvis, the external iliac artery (choice B) gives out two branches, the deep circumflex iliac and inferior epigastric arteries. The superior (choice E) and inferior (choice D) vesical arteries are branches of the internal iliac arteries, supplying the bladder.

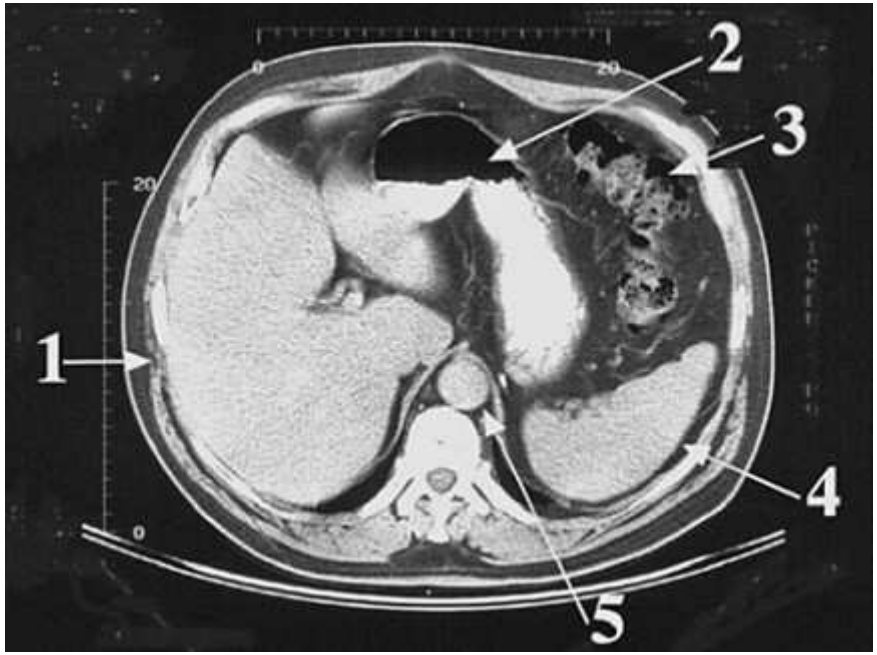
QUESTION 717
A 37-year-old rural female patient developed pain in the lower abdomen and pelvic regions. Her physician suspects a ruptured ectopic pregnancy. However, because of the isolation of the rural community, no medical imaging or laboratory procedure is available and the physician decides to perform a culdocentesis. In the latter procedure, the needle will aspirate from which of the following spaces?

A. ovarian fossa
B. rectouterine pouch
C. uterine body
D. uterine cervix
E. vesicouterine pouchAnswer:

Correct Answer: B
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
In culdocentesis, the needle is inserted through the posterior fornix of the vagina and fluid is aspirated from the rectouterine pouch. If nonclotting blood is collected then the likelihood of a ruptured ectopic pregnancy is high. This procedure is rapid and inexpensive, however, serum progesterone level assay or ultrasonography are preferred methods. The ovarian fossa (choice A) or vesicouterine pouch (choice E) are not used in culdocentesis. The uterine body (choice C) and cervix (choice D) would not reveal blood from a ruptured ectopic pregnancy and thus are also not used in culdocentesis.

QUESTION 718
Arrow 4 in following figure, is pointing to which of the following structures?



A. abdominal aorta
B. colon
C. liver
D. spleen
E. stomach

Correct Answer: D
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The spleen (arrow 4) lies to the left of the abdominal cavity. It is in contact with the left side of the stomach (arrow 2) and lodges against the left paravertebral gutter. The abdominal aorta (choice A, arrow 5) is seen as the circular structure immediately anterior to the vertebra. The colon (choice B, arrow 3) is the convoluted structure to the left anterior aspect of the abdominal cavity. The large liver (choice C, arrow 1) occupies most of the right side of the abdominal cavity.

The stomach (choice E, arrow 2) is located between the colon and the liver, and in this case, contains liquid contrast material.

QUESTION 719
An elderly resident of a nursing home fell down the front steps and subsequently became disoriented and lethargic. He is brought to the emergency room where an emergency MRI reveals that he has developed hydrocephalus due to a small hemorrhage obstructing the foramina of Monro. The foramina of Monro allow for communication between which of the following?

A. fourth ventricle and cerebral aqueduct
B. fourth ventricle and subarachnoid space
C. lateral ventricles and third ventricle
D. third ventricle and cerebral aqueduct
E. third ventricle and fourth ventricle

Correct Answer: C
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The foramina of Monro form the communication between the lateral ventricles and the third ventricle. The cerebral aqueduct of Sylvius flows caudally into the fourth ventricle (choice A). The lateral foramina of Luschka and the median foramen of Magendie allow for communication between the fourth ventricle and the subarachnoid space. The third ventricle communicates posteriorly with the cerebral aqueduct of Sylvius (choice D). Thus, the third and fourth ventricle communicate by way of this cerebral aqueduct.

QUESTION 720
Which of the following is the correct sequence of erythroid differentiation?

A. proerythroblast, basophilic erythroblast, polychromatophilic erythroblast, normoblast, reticulocyte, mature erythrocyte
B. proerythroblast, normoblast, reticulocyte, polychromatophilic erythroblast, basophilic erythroblast, mature erythrocyte
C. proerythroblast, polychromatophilic erythroblast, basophilic erythroblast, reticulocyte, normoblast, mature erythrocyte
D. proerythroblast, reticulocyte, normoblast, polychromatophilic erythroblast, basophilic erythroblast, mature erythrocyte
E. proerythroblast, reticulocyte, polychromatophilic erythroblast, normoblast, basophilic erythroblast, mature erythrocyte

Correct Answer: A
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:

The correct sequence of erythroid differentiation is indicated by choice A. Erythrocyte differentiation in the adult occurs exclusively in the bone marrow and consists of several cellular changes. The cell size decreases: proerythroblast 1419 m in diameter; basophilic erythroblast 1316 m; polychromatophilic erythroblast 1215 m; normoblast, reticulocyte, and mature erythrocyte 810 m. Condensation of the nuclear chromatin and decrease in nuclear diameter occur from the proerythroblast to the normoblast stage with ejection of the nucleus. Subsequent ejection of remaining organelles occurs in the reticulocyte to give rise to the mature erythrocyte. The maturing cells change their staining affinity because the increased hemoglobin in the cytoplasm results in increased acidophilia, whereas the decrease in the ribosome numbers in the cytoplasm results in decreased basophilia.
Choices B, C, D, and E are incorrect sequences.

QUESTION 721
In emphysema, which of the following components of the bronchioles is affected?

A. ciliated cuboidal epithelial cells
B. Clara cells
C. elastic fibers
D. goblet cells
E. squamous type I alveolar epithelial cells

Correct Answer: C
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
Elastic fibers are destroyed in emphysema by elastase. This protease is released by neutrophils recruited by macrophages under abnormal stimulus such as cigarette smoke. The loss of elasticity in the bronchioles and alveolar walls gives rise to emphysema, characterized by chronic airway obstruction. Ciliated cuboidal epithelial (choice A) and Clara (choice B) cells line the terminal bronchioles. Goblet cells (choice D) may be found at the beginning of the bronchioles and squamous type I alveolar epithelial cells line the respiratory bronchioles.

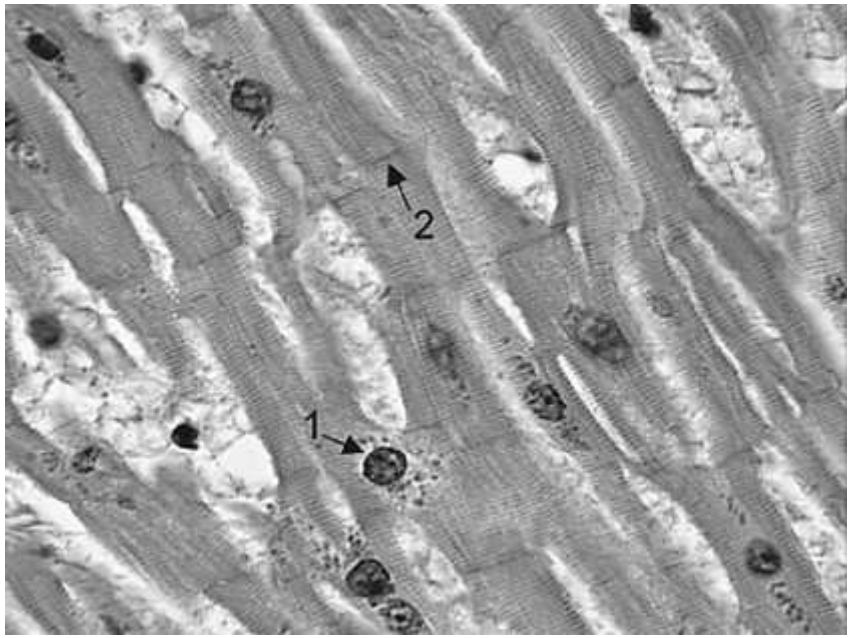
QUESTION 722
During development, the notochord grows in a cranial direction until it reaches the prechordal plate. This plate is the primordium of the oropharyngeal (or buccopharyngeal) membrane, which, in the embryo, will separate the stomodeum from the foregut. At 26 days of gestation, the oropharyngeal membrane will break down, allowing communication of the foregut with the oral cavity. Of the following structures in the adult, which one lies at the same location as the embryonic oropharyngeal membrane?

A. buccinators
B. palatoglossus
C. palatopharyngeus
D. stylopharyngeus
E. superior constrictor

Correct Answer: B
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The palatoglossus muscle, which can be observed in the oral cavity to form the palatoglossal arch anterior to the palatine tonsil, lies in the same location as the embryonic oropharyngeal membrane. It lies at the junction line between the stomodeum and the foregut. The buccinator (choice A) is a muscle of the cheek and thus is located in the original stomodeum. The palatopharyngeus (choice C) is located posterior to the palatoglossus and palatine tonsil, forming the palatopharyngeal arch. The palatopharyngeus, stylopharyngeus (choice D), and superior constrictor (choice E) muscles are all pharyngeal muscles and thus are located in the original foregut.

QUESTION 723
Referring to following figure, arrow 2 indicates which of the following structures?



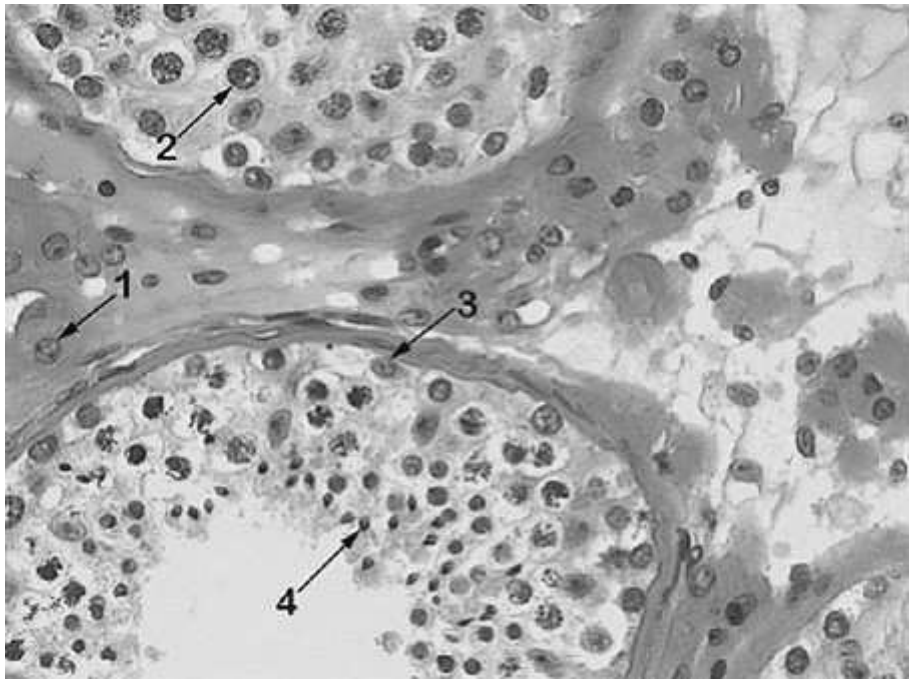
A. intercalated disk
B. motor end-plate
C. sarcoplasmic reticulum

D. tendinous junction
E. transverse tubule or T tubule

Correct Answer: A
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
The intercalated disks are specialized junctional complexes found only in cardiac muscle and they appear as dark lines between the muscle fibers. The motor end-plate (choice B) is a specialized group of synapses between the axon terminals of a motor neuron and the sarcolemma of a skeletal muscle fiber. It is not seen in cardiac muscle. The sarcoplasmic reticulum (choice C) is a specialized modification of the smooth endoplasmic reticulum for sequestering calcium ions. The transverse tubule or T tubule (choice E) is an invagination of the sarcolemma, which penetrates the muscle fiber and overlies the surface of the myofibrils. The sarcoplasmic reticulum and T tubule can only be seen in electron micrographs. There is no tendinous junction (choice D) in cardiac muscle.

QUESTION 724
The most common type of testicular cancer is germ cell carcinoma. However, testicular tumors arising from other cell types in the testis also occur. Arrow 1 in following figure, indicates which of the following structures?



A. Leydig cell
B. Sertoli cell
C. spermatid
D. spermatocyte
E. spermatogonia

Correct Answer: A
Section: Anatomy
Explanation

Explanation/Reference:
Explanation:
Arrow 1 indicates an interstitial cell of Leydig. These cells are recognizable by their location in the intertubular space, close to the capillaries and lymph vessels. Sertoli cells (choice B) are columnar cells with a large nucleolus. They span the distance from the seminiferous tubular wall to the lumen. However, their nuclei are located closer to the tubular wall. Spermatids (choice C; arrow 4) have a condensed nucleus, which becomes elongated with further maturation. This cell type is located closest to the lumen of the seminiferous tubule. Spermatocytes (choice D; arrow 2) are seen above the layer spermatogonia (choice E; arrow 3) which are located against the basal lamina.

QUESTION 725
Patients with functional dyspepsia (disturbed indigestion) and prominent nausea frequently experience spurts of excessive acid exposure to the upper duodenum. This results in pancreatic secretion, mainly through the action of which of the following substances?

A. cholecystokinin
B. gastrin
C. glucagon
D. secretin
E. vasoactive intestinal polypeptide (VIP)

Correct Answer: D
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
The strongest stimulator for the release of secretin from cells in the upper small-intestinal mucosa is the contact with acidic chyme. Increased serum secretin levels stimulate water and alkali secretions from the pancreas and the hepatic ducts and inhibit gastrin release. The release of pancreatic enzymes is stimulated by cholecystokinin (choice A). The most potent stimulators for the release of cholecystokinin are not acid, but digestion products of fat and protein. Strong stimulators for gastrin secretion (choice B) are vagus nerve excitation, distention of the stomach, and protein digestion products. Gastrin then stimulates acid secretion and

mucosal growth. The major effect of glucagon (choice C) is to increase blood glucose levels. Hence, it is secreted in response to hypoglycemia and protein digestion products, which are then used for gluconeogenesis. VIP (choice E) indeed stimulates intestinal and pancreatic secretion. However, it acts as neurotransmitter in the enteric nervous system and is mainly released by mechanical and neuronal stimulation.

QUESTION 726
A 41-year-old male suffering from unstable angina is undergoing cardiac testing. At rest, his heart rate is 70 beats per minute. His left ventricular end-diastolic volume is estimated to be 150 mL, while his end systolic volume is 80 mL. What is his estimated cardiac output?

A. 3900 mL/min
B. 4400 mL/min
C. 4900 mL/min
D. 5400 mL/min
E. 5900 mL/min

Correct Answer: C
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
Cardiac output is calculated by multiplying heart rate by stroke volume. Stroke volume is the difference between end-diastolic ventricular volume and end-systolic volume. Hence 150 - 80 = 70 mL stroke volume. 70 mL × 70 beats/min = 4900 mL/min.

QUESTION 727
A dislocated shoulder of a middle-aged man was corrected under conscious sedation with etomidate. Since etomidate has been reported to affect adrenocortical function as a side effect, the patient's ACTH and cortisol were measured in blood samples taken at the indicated times on the following day. What do the ACTH results indicate?

	Normal values	Patient 7 a.m.	Patient 7:30 a.m.	Patient 7 p.m.	Patient 7:30 p.m.
ACTH (pg/mL)	50–250	110	90	120	200
Cortisol (ug/dL)	6–23	10	8	20	24

A. inverted circadian pulsatile release
B. normal circadian pulsatile release
C. normal circadian non-pulsatile release

D. primary adrenal insufficiency
E. secondary adrenal insufficiency

Correct Answer: A
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
The differences in the hormone concentrations of blood samples taken half-an-hour apart indicate pulsatile release. Hence, non-pulsatile release (choice C) is excluded. However, the normal circadian rhythm for ACTH (choice B) is likely to be highest early in the morning, with cortisol production following ACTH by a short delay, opposite to the patient's values. Such a reversed pattern could, for instance, be observed for night workers and is not likely to be caused by etomidate. Etomidate has been associated with suppression of glucocorticoid and mineralcorticoid synthesis in the adrenal cortex. Substantial damage to the adrenal gland might indeed lead to adrenocortical hypofunction, called Addison disease. However, primary adrenal insufficiency (disorder of the gland, choice D), and secondary adrenal insufficiency (inadequate ACTH secretion, choice E) both present with low levels of cortisol.

QUESTION 728
A biopsy from a 55-year-old woman with breast cancer was submitted to an estrogen receptor assay. The binding of estrogen to the cancer cells below figure, solid line was plotted in the form of a Scatchard plot and compared to control cells below figure, dotted line). Which of the following would you conclude for the patient's estrogen receptors?

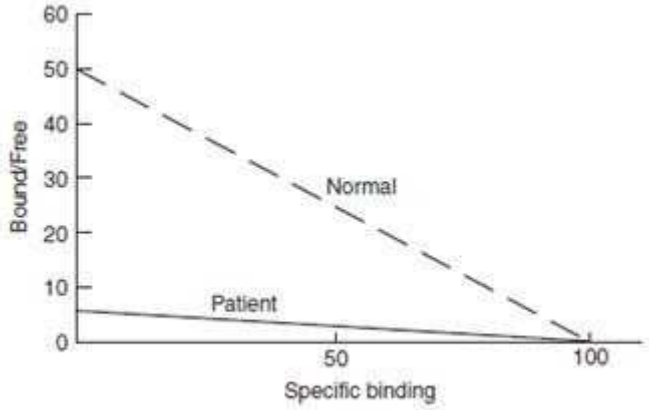


FIG. 2-4

A. they are equal in number and have a higher affinity
B. they are equal in number and have a lower affinity
C. they are fewer in number and have a higher affinity

D. they are fewer in number and have a lower affinity
E. they are higher in number and have an equal affinity

Correct Answer: B
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
The slope of the patient's line is decreased compared to normal. This indicates a low affinity of estrogen for the estrogen receptor, which makes choice B correct and choice Aincorrect. The x- intercept is called Bmax and represents the total number of estrogen receptors. This is unchanged in the patient compared to normal so that choices C, D, and E are excluded. The information about the numbers and status of estrogen and progesterone receptors on cancer cells is of high clinical value to determine the efficiency of consequent hormonal therapy.

QUESTION 729
A 71-year-old man was admitted to the hospital after getting very dizzy upon rising from the toilet seat. At that time his pulse was racing and he remembers that his stool looked very different than usual. Over the last 4 or 5 weeks before the incident, the patient self-medicated with high-dose ibuprofen three times a day to control some pain in his hips. What is the mechanism of action for nonsteroidal anti-inflammatory drugs (NSAIDs) to cause gastrointestinal (GI) bleeding?

A. they inhibit arachidonic acid synthesis
B. they inhibit bradykinin synthesis
C. they inhibit cyclooxygenase
D. they inhibit histamine synthesis
E. they promote prostaglandin synthesis

Correct Answer: C
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
NSAIDs inhibit cyclooxygenase and consequently inhibit (not promote, choice E) synthesis of prostaglandins. In the stomach, prostaglandins have a cytoprotective effect through inhibition of acid secretion, enhancement of mucosal blood flow, and stimulation of bicarbonate and mucus secretion. Inhibiting these processes can cause stomach ulcers and bleeding such as described in the case. Arachidonic acid (choice A) is not directly affected by NSAIDs--it is turned into prostaglandin by

H_2

the action of cyclooxygenases. NSAIDs do not regulate bradykinin and histamine synthesis (choices B and D).

QUESTION 730

A 52-year-old man has a history of anginal pain that until recently was responsive to nitrates. He is now evaluated for possible angioplasty. The graph in below figure shows the ECG of this patient. Blood flow across the mitral valve is largest around which indicated point in this ECG tracing?

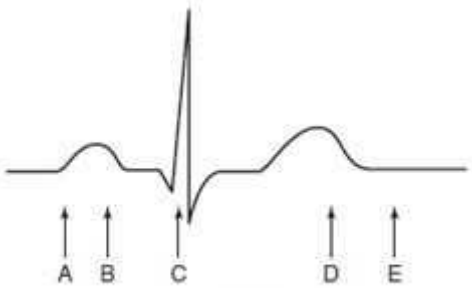


FIG. 2-5

A. A
B. B
C. C
D. D
E. E

Correct Answer: E
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
The most rapid filling of the ventricles occurs in early diastole, immediately after opening of the atrioventricular valves. This happens after the repolarization phase (T wave) and resulting relaxation of the cardiac ventricular muscle. Excitation of the atria (choice A) also results in increased blood flow into the ventricles, occurring around choice B. However, the flow at that time is less than during early diastole. Ventricular contraction begins with the QRS complex (choice C) and lasts until the end of the T wave (choice D). During this time, the mitral and tricuspid valves are closed.

QUESTION 731
The graph in below figure shows the pressurevolume curve of the left ventricle of this patient (shaded area). The pressurevolume curve of a normal subject is shown for comparison (broken lines). Compared to normal, which term best describes this patient's heart?

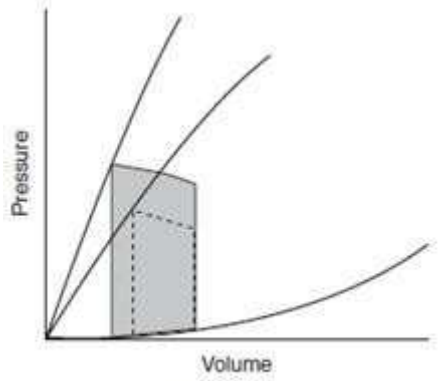


FIG. 2-6

A. decreased afterload
B. decreased preload
C. decreased stroke volume
D. increased force of contraction
E. increased preload

Correct Answer: D
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
Note that the end-diastolic volume of this patient is the same as that of a normal subject. Because the patient's stroke volume is larger than that of a normal subject, the force of contraction must also be larger. This could be due to increased sympathetic tone or to the fact that the patient took inotropic medications. The volume remaining after the ventricular contraction is correspondingly smaller compared to normal. Preload (choices B and E) equals end-diastolic volume and is the same in the patient and normal subjects. Afterload (choice A) is equal to arterial pressure. Both afterload and stroke volume (choice C) are larger in this patient compared to normal.

QUESTION 732
The graph in below figure shows the jugular vein pressure curve of this patient. If the first heart sound occurs between letters C and D, which part of the curve represents the atrial contraction?

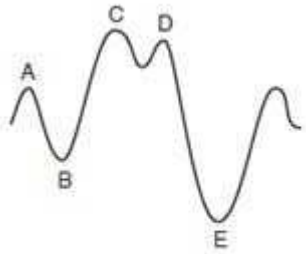


FIG. 2-7

A. peak A
B. peak C
C. peak D
D. trough B
E. trough E

Correct Answer: B
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
below figure shows the jugular vein pressure curve. Pressure in the jugular vein reflects atrial pressure and is highest during the atrial contraction (named the "a wave"). The "v wave" (choice A) represents the rise in atrial pressure before the tricuspid valve opens during diastole. The "y notch" (choice D) is due to the fall in atrial pressure during the ventricular filling phase. The "c wave" (choice C) is due to the rise in atrial pressure produced by the bulging of the tricuspid valve during isovolumetric contraction of the right ventricle. The "x notch" (choice E) coincides with the ventricular ejection phase.

QUESTION 733
A 14-year-old boy presents with weight loss and diarrhea. His tongue becomes sore and blistery after eating oatmeal or rye bread, which leads to the diagnosis of celiac disease. The boy and his parents are advised to be sensitive to symptoms of tetany and paresthesias, since they can occur as a consequence of malabsorption of which of the following?

A. calcium
B. carbohydrates
C. fat
D. iron
E. water

Correct Answer: A
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
In patients with celiac disease the protein gluten, which is found in bread, oats, and many other foods containing wheat, barley, or rye, triggers an autoimmune response that causes damage to the small intestine leading to widespread manifestations of malabsorption. Calcium is difficult to absorb, so patients frequently experience symptoms of hypocalcemia such as muscle cramping, titanic contractions, numbness, and tingling sensations. For sensory and motor nerves, calcium is a critical second messenger involved in normal cell function, neural transmission, and cell membrane stability. The nerves respond to a lack of calcium with hyperexcitability. The inability to absorb nutrients such as carbohydrates (choice B) leads to weight loss as experienced by the boy. Fat malabsorption (choice C) is not uncommon in patients with celiac disease as a consequence of greatly diminished absorptive surface. It would manifest in steatorrhea. Iron (choice D), like calcium, is difficult to absorb and may lead to anemia. The general decrease in electrolyte absorption leads to decreased water absorption (choice E). The increased osmotic load in the GI lumen accounts for the boy's diarrhea.

QUESTION 734
An adult male becomes hypotensive during surgery because of blood loss. Intravenous administration of 500 ml of which of the following solutions will have the greatest effect in restoring blood volume, and thus blood pressure to normal?

A. blood plasma
B. distilled water
C. hypoosmotic NaCl
D. isotonic dextrose solution
E. isotonic saline solution

Correct Answer: A
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
Intravenous solutions are distributed in the various body fluid compartments based on osmolality and their ability to penetrate the vascular wall and the cell membrane. The proteins in blood plasma will remain within the vascular compartment because of their low permeability across the vessel wall. Thus, 500 mL of blood plasma will remain in the vascular compartment. Water (choice B) passes across the cell membrane and the vascular wall easily. Hence distilled water will distribute itself between cellular and extracellular spaces, meaning only a small portion will actually contribute to blood volume, the other choices (C, D, and E) cross the vascular barrier and distribute partially to the extravascular space and thus are less effective intravascular volume expanders.

QUESTION 735
Using laboratory micropuncture technique, blood plasma is collected from both the afferent arteriole and efferent arteriole of a renal cortical glomerulus. Which of the following has the lowest afferent/efferent arteriole concentration ratio?

A. albumin
B. chloride
C. glucose
D. potassium
E. sodium

Correct Answer: A
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
The process of glomerular ultrafiltration creates a tubular fluid that is essentially protein free. Hence, as plasma passes from the afferent arteriole, through the glomerular capillaries to the efferent arteriole, the protein albumin concentration rises as approximately 20% of the fluid is filtered out, leaving the albumin behind, giving an afferent/efferent arteriole concentration ratio of approximately 0.8. By contrast, the glomerular capillary membrane is freely permeable to water and other small particles such as glucose (choice A), chloride (choice B), potassium (choice D), and sodium (choice E), so their concentrations do not change as approximately 20% of water and solute are filtered into Bowman's capsule, giving afferent/ efferent arteriole concentration ratios of 1.0.

QUESTION 736
It is known that stretch receptors contained in the walls of the atria convey nerve impulses to the brainstem via the vagus nerve. Under normal conditions, these nerve impulses are most likely to occur during ventricular systole. What information is communicated to the brain by these nerve impulses?

A. arterial muscle contraction
B. diastolic arterial pressure
C. filling of the atrium by venous pressure
D. filling of the ventricle
E. systolic arterial pressure

Correct Answer: C
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
The atrial stretch receptors are depolarized by stretch of the atria proportional to the magnitude of venous-filling pressure. The frequency of action potentials rises to a maximum at the peak of the atrial "v" wave, which signals maximum atrial filling during ventricular contraction. Although the remaining choices (A, B, D, and E) may be influenced by the filling of the heart by venous pressure, the information conveyed to the brain via the atrial stretch receptors relates directly to the filling pressure of the atria themselves.

QUESTION 737
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

Correct Answer: D
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
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.

QUESTION 738
A 53-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

Correct Answer: B
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
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 A and C).

QUESTION 739
Exhibit:

A. carbamino compounds
B. CO_2 dissolved in solution
C. CO_3^{-2}
D. HCO_3^-
E. H_2CO_3

Please refer to the exhibit.
The majority of in the blood is carried in which of the following forms?

CO_2

A. A
B. B
C. C
D. D
E. E

Correct Answer: D
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
reacts with to form (carbonic acid), in a reaction catalyzed by carbonic anhydrase.

CO_2

Carbonic acid then dissociates to form -. Approximately 90% of the total in the blood is

HCO_3

carried as -. rapidly dissociates after being formed and a negligible fraction of blood

HCO_3

is carried in this form (choice D). Some is carried bound to hemoglobin, as carbamino

CO_2

compounds (choice A). This is a small fraction of the total (5%). Asimilar small fraction (5%) of

CO_2

total remains dissolved in solution (choice B). Given that normal blood pH is near 7, essentially

CO_2

dissociates to form (choice C).

HCO_3^-

QUESTION 740
A patient with acute glomerulonephritis has a total plasma of 2.5 mmol/L and a GFR of 160

Ca^{2+}

L/day. What is the estimated daily filtered load of calcium?

A. 64 mmol/day
B. 120 mmol/day
C. 240 mmol/day
D. 400 mmol/day
E. 800 mmol/day

Correct Answer: C
Section: Physiology

Explanation

Explanation/Reference:
Explanation:
About 40% of total plasma is bound to proteins and not filtered at the glomerular basement

Ca^{2+}

membrane. Therefore, the estimated daily filtered load is 1.5 mmol/L × 160 L/day = 240 mmol/day. The exact amount of free versus total depends on the blood pH: free increases during

Ca^{2+}

acidosis and decreases during alkalosis. None of the other choices (A, B, D, and E) reflect the correct renal calcium filtration load.

QUESTION 741
Lack of oxygen (hypoxia) will cause reflex vasoconstriction in the circulation supplying which of the following organs?

A. brain
B. heart muscle
C. kidney
D. lungs
E. skeletal muscle

Correct Answer: D
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
Local hypoxia causes vasoconstriction in vessels of the pulmonary circulation. This is an adaptive response, since it will shunt blood away from poorly ventilated alveoli. This response differentiates the pulmonary circulation from the vasculature of other organs. In heart muscle, skeletal muscle, kidney, and brain (choices A, B, C, and E) vasodilation occurs in response to local hypoxia.

QUESTION 742
Lipoxygenase converts arachidonic acid to biologically active compounds called leukotrienes. Leukotrienes have been implicated in several disease entities, including allergic asthma, where they are presumed to mediate bronchoconstriction. Introducing leukotrienes into an airway would be expected to cause which of the following responses?

A. decreased airway resistance
B. decreased dead space volume
C. increased functional residual capacity (FRC)
D. increased lung compliance
E. increased total lung capacity

Correct Answer: B
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
Bronchiole volume contributes to dead space volume, so increasing bronchoconstriction would decrease bronchiolar volume and thus decrease dead space volume. Bronchoconstriction is a major determinant of airway resistance to air flow. Leukotrienes, by increasing airway constriction, would increase resistance to air flow (choice A). Lung elastic tissue and alveolar surface tension determine lung compliance (choice D), which should not be affected by airway leukotrienes exposure. FRC (choice C), the point of mechanical balance between chest wall and lung, is dependent on lung compliance and, similarly, would not be affected by leukotrienes exposure. Any bronchoconstriction would slightly decrease total lung capacity (choice E).

QUESTION 743
Below figure shows the amounts of water ingested and secreted daily into the GI tract by a healthy individual. Since about 100 mL of water is excreted daily in the stool, which of the following volumes (in milliliter) best reflects the daily absorbed water in the indicated areas x, y, and z of the GI tract?

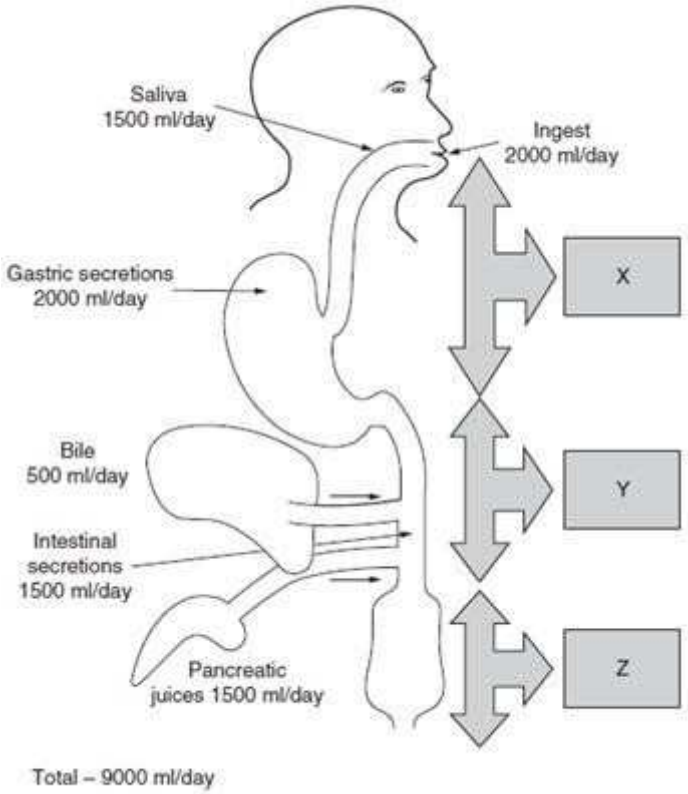


FIG. 2-8

	X	Y	Z
A.	0	400	8500
B.	0	8500	400
C.	450	450	8000
D.	450	8000	450
E.	8000	450	450

A. Option A
B. Option B
C. Option C
D. Option D
E. Option E

Correct Answer: B
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
The small intestine absorbs massive quantities of water. Anormal person takes in about 2 L of fluid every day. Another 7 L of fluid are received by the small intestine daily as secretions from salivary glands (1.5 L), stomach (2 L), pancreas (1.5 L), liver (0.5 L), and the small intestine itself (1.5 L). That results in a total of about 9 L of fluid entering the GI tract daily. In a healthy person the duodenum, jejunum, and ileum absorb the bulk of the water that enters the GI tract, here 8500 mL. The colon absorbs most of the remaining fluid (400 mL), not the bulk of it (choice A) and excretes about 100 mL daily. There is generally no water absorption in the esophagus and stomach. Therefore, choices C, D, and E are incorrect.

QUESTION 744
Exhibit:

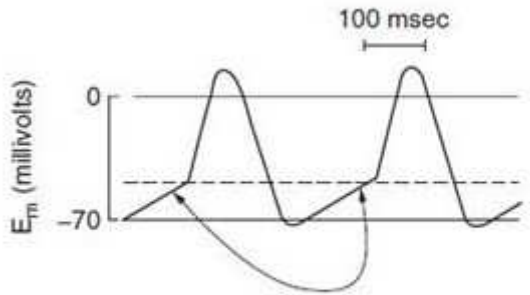


FIG. 2-9

The action potentials shown in below figure represent those of which kind of cells?

A. cardiac nodal cells
B. myelinated motor axons
C. sensory neurons

D. skeletal muscle cells
E. ventricular Purkinje cells

Correct Answer: A
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
The action potentials illustrated must be those of cardiac nodal cells (SA node or AV node). The duration of these action potentials is too long for motor axons, (choice B), sensory neurons (choice C), or skeletal muscle fibers (choice D). Also, the configuration is different and a pacemaker potential is clearly present. They cannot be ventricular Purkinje action potentials (choice E) because these have a more negative diastolic component that does not gradually depolarize, a longer duration (200 msec) and a plateau region.

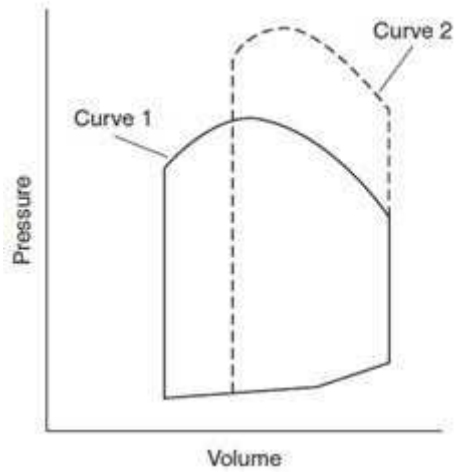
QUESTION 745
Apatient is admitted to the hospital following a knife wound to the abdomen which results in extensive bleeding into the abdomen. The arterial pressure at admission is 65/30 mm Hg with a rapid, weak pulse. Compared to normal, the nerve impulses in the carotid sinus nerves and in the sympathetic nerves are changed in what way?

A. both show decreased nerve impulse rates
B. both show increased nerve impulse rates
C. carotid sinus nerve impulses are decreased, sympathetic are increased
D. carotid sinus nerve impulses are increased, sympathetic are decreased
E. the patient is unconscious so there are no changes in nerve impulse rates

Correct Answer: C
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
The carotid sinus baroreceptors signal the magnitude of arterial pressure to the brainstem which then causes reflex inhibition of sympathetic nerves to the body. Thus, a decrease in arterial pressure will cause a reduced carotid sinus nerve impulse rate, which reflexly increases sympathetic nerve impulse rates. Hence, choices A, B, and D are directionally incorrect. Choice E is incorrect because the arterial baroreflexes function at the level of the brainstem, which does not require the conscious mind for its action.

QUESTION 746
A 66-year-old woman is undergoing surgery to repair an abdominal aortic aneurism. During the procedure the abdominal aorta is momentarily clamped below the renal arteries. below figure shows the left ventricular pressure/ volume relationship immediately before (curve 1) and during (curve 2) the aortic occlusion. The change in curve 2 represents an increase in which of the following?



A. afterload
B. cardiac output
C. ejection fraction
D. preload
E. stroke volume

Correct Answer: A
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
Clamping of the abdominal aorta suddenly increases peripheral vascular resistance to blood flow. Hence aortic pressure suddenly rises to a high level. This represents an increased afterload, that is, an increased ventricular pressure is required to eject blood into the aorta. below figure shows that momentary clamping of the aorta does not alter the preload, that is, the filling of the ventricle during diastole (choice D). below figure shows that the inverse relationship between afterload and stroke volume causes a reduced stroke volume (choice E) immediately after aortic clamping. Since end- diastolic volume (preload) is unchanged, while stroke volume is decreased, this represents a decreased ejection fraction (choice C). Cardiac output is calculated as stroke volume X heart rate. Since heart rate is not given, the cardiac output cannot be determined (choice B). However, it is likely, by Ohm's law that a momentary rise in peripheral vascular resistance will decrease cardiac output.

QUESTION 747
In below figure, which point depicts the excreted glucose in a 31-year-old woman with untreated nephrogenic diabetes insipidus?

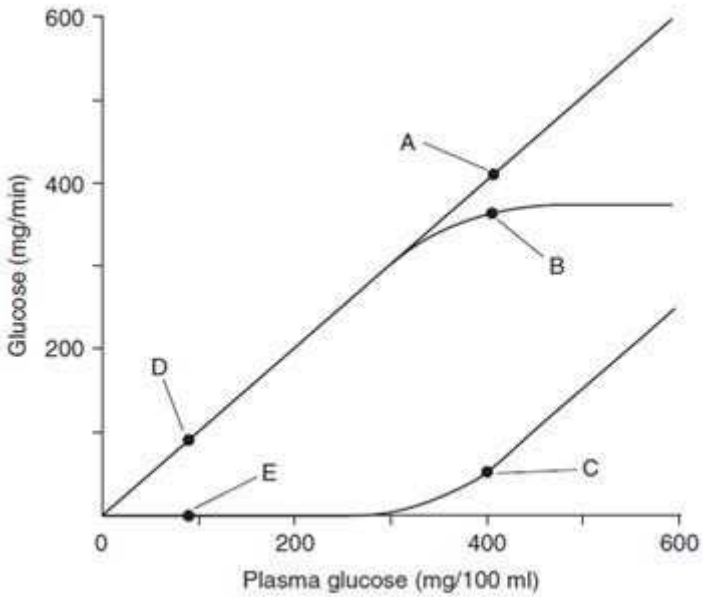


FIG. 2-11

A. A
B. B
C. C
D. D
E. E

Correct Answer: E
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
Nephrogenic diabetes insipidus is a condition in which the kidney is insensitive to the normal action of ADH, which is to cause a concentrated urine by promoting water reabsorption in the collecting duct. In such a person, plasma glucose will be normal--around 80 mg/ 100 mL and excreted glucose will be zero, since the tubular maximum for glucose has not been exceeded and all the filtered glucose is normally reabsorbed. Choices A, B, and C depict the filtered, reabsorbed, and excreted glucose in a hyperglycemic state which might occur during diabetes mellitus. Choice D depicts the filtered and reabsorbed glucose in a fasting, normoglycemic state.

QUESTION 748
Exhibit: *missing*
In below figure, which point depicts the renal filtered glucose in an 11-year-old male with untreated Type I diabetes mellitus?

A. A
B. B
C. C
D. D
E. E

Correct Answer: A
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
Type I diabetes mellitus is a condition in which the pancreas secretes inadequate quantities of insulin, causing a fasting hyperglycemia. Choice Adepicts the filtered glucose in such a hyperglycemic state. Choices B and C depict the reabsorbed and excreted glucose which would also occur in a hyperglycemic state. Choice D depicts the filtered and reabsorbed glucose in a fasting, normoglycemic state. Choice E depicts the zero excreted glucose that would occur in a fasting nondiabetic individual since the tubular maximum for glucose has not been exceeded.

QUESTION 749
A 57-year-old woman presents with an arterial pressure of 180/115 mm Hg, and blood creatinine levels are elevated. Renal angiography reveals a severe bilateral stenosis of the renal arteries. Which of the following are elevated also?

A. ADH secretion
B. GFR
C. para-aminohippurate (PAH) clearance
D. renin secretion
E. urine output

Correct Answer: D
Section: Physiology
Explanation

Explanation/Reference:
Explanation:
The bilateral renal artery stenosis will reduce renal perfusion pressure. Hence the juxtaglomerular apparatus will greatly increase renin secretion which causes the

large rise in arterial pressure because of the vasoconstrictor action of angiotensin II. A reduced renal perfusion pressure will decrease PAH clearance (choice C), which estimates renal blood flow and will reduce GFR (choice B). The decreased formation of tubular fluid will result in reduced urine output (choice E) and the large rise in arterial pressure will activate arterial baroreceptors and suppress ADH secretion from the posterior pituitary (choice A).

QUESTION 750
A 37-year-old man was immunologically competent but presented to his physician with malaise, fever, lethargy, and back pain. Examination also revealed vertebral osteomyelitis, splenomegaly, and hepatomegaly. He was a PPD-negative farm worker who consumed unpasteurized goat milk. Which of the organisms listed below is the mostlikely etiological agent?

A. Actinomyces israelii
B. Aspergillus fumigates
C. Brucella melitensis
D. Candida albicans
E. Mycobacterium tuberculosis

Correct Answer: C
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
B. melitensis is a gram-negative aerobic bacillus that grows well in the presence of 10% C as a

O_2

coccobacillus. This microbe has a predilection for the cells of the reticuloendothelial system. This explains the frequent splenomegaly or hepatomegaly, which when present provide useful clues for the diagnosis of brucellosis. M. tuberculosis (choice E) is a strictly aerobic acidfast rod. It can cause tuberculosis and vertebral osteomyelitis. In these cases and in the absence of immunosuppression, the Mantoux test (PPD-based) is positive. A. israelii (choice A) is a gram-positive branching rod that causes actinomycosis. A. fumigatus (choice B) is a branching, filamentous fungus that has been associated with invasive infections in immunocompromised hosts. Candida albicans (choice D) is a yeast that causes disseminated disease in immunosuppressed individuals.

QUESTION 751
A 45-year-old man was admitted to the hospital because of fever, shortness of breath, and weight loss with edema in the lower limbs. Examination revealed cardiomegaly and arrhythmias, and a diagnosis of myocarditis was made. Bacterial blood cultures were negative. Which of the following organisms is most likely responsible for this illness?

A. adenovirus
B. coxsackie group A virus
C. coxsackie group B virus

D. mumps virus
E. rhinovirus

Correct Answer: C
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
Myocarditis is most commonly caused by Coxsackie group B viruses, and may be preceded by gastrointestinal or respiratory symptoms. The mumps virus (choice D), coronaviruses (choice B), adenovirus (choice A), and rhinovirus (choice E) may be associated with influenza like, or gastrointestinal symptoms, but they are not common causes of myocarditis.

QUESTION 752
A 5-month-old baby presents to the local community clinic with noted oral candidiasis, chronic diarrhea, extensive diaper rash, and an overall failure to thrive. Previously this infant has been seen for multiple severe, recurrent infections from viruses, fungi, bacteria, and protozoa. Chest x-ray reveals an absent thymic shadow. Which of the following immunodeficiencies best explains this baby's recurrent infections?

A. Bruton agammaglobulinemia
B. deficiencies in the C5C8 components of complement
C. deficiency in neutrophil NADPH oxidase
D. DiGeorge syndrome
E. severe combined immunodeficiency (SCID)

Correct Answer: E
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
The most serious immunodeficiency is severe combined immunodeficiency disease (SCID). This occurs as a result of a defect in early stem differentiation resulting in an acute deficiency in both T and B cells. Severe and recurrent infections occur early in life from bacteria, viruses, fungi, and protozoa. DiGeorge syndrome (choice D) is due to poor development of thymus that leads to a pronounced deficiency of T cells. In Bruton agammaglobulinemia (choice A) there is virtual absence of B cells and extremely low levels of immunoglobulins. Deficiencies in complement components C5 through C8 (choice B) are associated with enhanced susceptibility to N. gonorrhoeae and N. meningitides. In chronic granulomatous disease (CGD) there is increased susceptibility to infection by S. aureus, or enteric rods. CGD is due to a deficiency in neutrophilic NADPH oxidase, which is associated with the microbiocidal activity of neutrophils (choice C).

QUESTION 753
Which of the following can most likely restore the immunological competency of this 5-month-old baby?

A. administration of purine nucleoside phosphorylase
B. B-cell supplementation
C. compatible bone marrow transplantation
D. injection of adenosine deaminase
E. T-cell treatment

Correct Answer: C
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
In patients with combined B- and T-cell immunodeficiencies, compatible bone marrow transplantation, from an HLA-identical sibling, can restore immunological competence for bacteria, viruses, fungi, and protozoa. Administration of adenosine deaminase or purine nucleoside phosphorylase may sometimes reduce the number and severity of microbial infections by a slight, temporary stimulation of the production of B and T cells, but it does not restore immunity to microorganisms (choices Aand D). Treatment with compatible B or T cells may provide very brief humoral or cellular immunity (choices Band E).

QUESTION 754
A 20-year-old woman with generally normal health and immune capacity visited her doctor complaining of 2 weeks of fever, sore throat, and cough. She had recently seen bloodstreaked sputum and had noticeable chest pain. X-rays showed only a moderate amount of pulmonary consolidation, while a cold agglutinin titer of 1:256 was reported. Which organism listed below is the most likely etiological agent?

A. Chlamydia pneunoniae
B. Coxiella burnetii
C. Legionella pneumophila
D. Mycoplasma pneumonia
E. Pneumocystis carinii

Correct Answer: D
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
"Walking" primary atypical pneumonia caused by M. pneumoniae can lead to formation of IgM antibodies called cold agglutinins, because they agglutinate type O human erythrocytes at 4℃. L. pneumophila (choice C), C. burnetii (choice B), P. carinii (choice E), and C. pneumoniae (choice A) may produce symptoms of pneumonia similar to those induced by M. pneumoniae, but normally these microbes are not associated with cold agglutinin formation.

QUESTION 755

A medical student has been immunized with hepatitis B virus (HBV) recombinant vaccine. The curve in below figure represents the production of protective antibodies to the viral component present in the recombinant vaccine. Which of the following is the known viral component of the HBV vaccine?

A. nucleocapsid proteins of HBV
B. RNA genome of HBV
C. viral core antigen (HBcAg)
D. viral e antigen (HBeAg)
E. viral surface antigen (HBsAg)

Correct Answer: E
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
The envelope of hepatitis B virus contains an antigen known as HBsAg (hepatitis B surface antigen). This antigen is of importance because production of antibodies to HBsAg indicates immunity against hepatitis B virus, which resulted either from infection or vaccination with HBsAg. Treatment of HBV with a nonionic detergent removes the envelope and produces the viral core, which contains the hepatitis B core antigen (HBcAg). Antibodies to HBcAg are not protective (choice C). Treatment of the viral core with strong detergents results in the release of a soluble core antigen called hepatitis virus antigen e (HBeAg). Production of antibody to HBeAg signals active disease during which the patient is infectious (choice D). The DNA genome (choice B), or the nucleocapsid proteins of HBV (choice A) are not protective.

QUESTION 756
While on a wilderness vacation, a banker develops extensive skin lesions noted for their varying degrees of erythema, edema, and vesiculations. His physician tells him that these lesions are due to delayed type hypersensitivity. If this is actually the case, which of the following statements is accurate?

A. Delayed-type hypersensitivity can be transferred passively to volunteers by sensitized lymphocytes.
B. Delayed-type hypersensitivity is suppressed by antihistaminic drugs.

C. This allergy does not cause tissue damage.
D. This allergy is due to IgE absorbed on mast cells.
E. This type of allergy usually occurs after inhalation of grass pollens.

Correct Answer: A
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
Delayed-type hypersensitivity is mediated by helper CD4 lymphocytes, not antibody (choice D). Thus it can only be transferred by sensitized CD4 helper lymphocytes. Sensitization occurs via such substances as poison ivy, poison oak, some cosmetics, topically applied sulfonamides, or other drugs and simple chemicals, such as nickel, formaldehyde, and others, but not inhalation of grass pollen (choice E). Part of the tissue destruction seen in tuberculosis is due to delayed-type hypersensitivity, so this type of hypersensitivity reaction may lead to tissue damage (choice C). Administration of antihistaminic drugs, epinephrine, or cromolyn sodium is used for the treatment of anaphylactic reactions resulting from type I hypersensitivity, but not delayed-type hypersensitivity (choice B).

QUESTION 757
A 42-year-old woman had a catheter placed in her urethra. One week later she is experiencing suprapubic flank pain with urinary urgency and frequency. She has also chills and fever. After examining the patient and evaluating the sediment of her centrifuged urine, she is informed by her physician that she has acute ascending pyelonephritis. If the diagnosis is accurate and the patient's urine is cultured, which of the following organisms will most likely be isolated?

A. Clostridium difficile
B. Escherichia coli with pili
C. Pseudomonas aeruginosa
D. Staphylococcus aureus
E. streptococci--group B

Correct Answer: B
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
Piliated strains of E. coli move up the urethra to infect the bladder and kidney. Infections of the kidney cause pyelonephritis. The vast majority of cases of bacterial pyelonephritis, cystitis, and other urinary tract infections are caused by E. coli. Introduction of catheters into the urethra has been associated with the occurrence of urinary tract infections. C. difficile is the cause of pseudomembranous colitis (choice A). S. aureus is usually the cause of boils, skin sepsis, postoperative wound infections, scalded skin syndrome, food-borne infection, septicemia, endocarditis, toxic shock syndrome, osteomyelitis, and pneumonia (choice D). P. aeruginosa is usually the cause of infections of skin and burns. It is also the major pathogen in cystic fibrosis, and can cause urinary infections, but not as commonly as E. coli (choice C). Group B streptococci (choice E) are usual vaginal flora, not pathogenic to the host but may be opportunistic to newborns.

QUESTION 758
A 25-year-old female executive presents with edema, hematuria, proteinuria, and decreased urination indicative of glomerulonephritis. Three weeks ago she had impetigo on her chest which resolved without treatment. Which of the following organisms is the most likely cause of her renal disease?

A. E. coli
B. S. aureus
C. S. saprophyticus
D. Streptococcus agalactiae
E. S. pyogenes

Correct Answer: E
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
Acute glomerulonephritis appears as a complication after pharyngeal or skin infections with Group A S. pyogenes. Patients with poststreptococcal glomerulonephritis develop high levels of antibodies against streptolysin O of S. pyogenes. While S. aureus (choice B) may also cause impetigo, it is seldom, if ever, found to be the cause of postinfectious glomerulonephritis. None of the other organisms (choices A, C, or D) have been identified with this postinfectious complication either.

QUESTION 759
A 22-year-old man complains to his family physician of fatigue, night sweats, and a dry unproductive cough. Until the past few months, he had apparently been in good health. Acomplete blood count (CBC) and differential blood count reveal that he is lymphopenic. X-ray examination reveals an interstitial pneumonia. Skin test reactions to a battery of materials are normal. Which of the following should be the next step in evaluating this patient's illness?

A. CH50 complement assay
B. chemotaxis assay
C. identification of the organism that is causing the pneumonia
D. intracellular killing assay
E. nitroblue tetrazolium reduction assay

Correct Answer: C
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
The patient described in the question probably has AIDS. Such individuals will be lymphopenic and have greatly reduced immunity. AIDS victims commonly develop

P. carinii pneumonia. The most important evaluative procedure for the patient described is determining the cause of the pneumonia so the problem can be corrected. Identifying the infecting organism may assist in the overall diagnosis. Choices A, B, D, and E involve innate immunity; either complement activity or phagocytic cell functions, and thus, would not be of much diagnostic assistance.

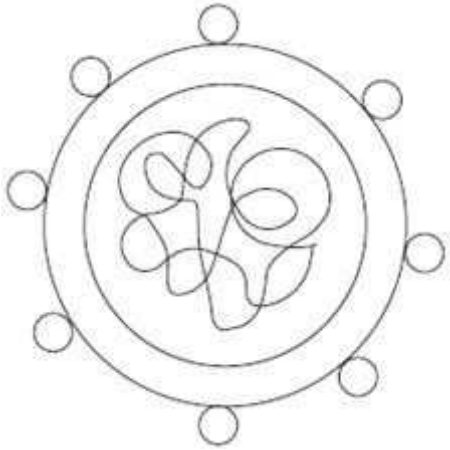
QUESTION 760
A 22-year-old Hispanic man worked for a company that processed animal products and provided no medical coverage benefits. One week after working with wool imported from a Caribbean island, he developed a small lesion on his arm resembling an insect bite. One week later, the lesion was 2.5 cm in diameter with a central, black sloughed-skin area. Two weeks later, he presented at an emergency room with early stages of sepsis. Which of the following microbes is responsible for the infection?

A. Bacillus anthracis
B. Bacteroides melanogenicus
C. Hemophilus ducreyi
D. M. scrofulaceum
E. Treponema pallidum

Correct Answer: A
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
A patient with cutaneous anthrax usually presents with a pruritic macule or papule that enlarges into a round ulcer in several days. Then 12 mm vesicles that discharge clear or sanguinous fluid might appear. Purulent drainage ordinarily does not occur. This is followed by the development of a painless, depressed, blackcolored eschar. If it is not treated early, dissemination of the disease in about 10% of cases results in septicemia and meningitis. H. ducreyi (choice C) produces a disease called chancroid or soft chancre, which is not associated with the formation of black eschars. T. pallidum (choice E) produces hard chancres without black eschars. B. melanogenicus (choice B) causes abscesses. M. scrofulaceum (choice D) is associated with scrofula which is cervical adenitis.

QUESTION 761
An outbreak of severe, atypical pneumonia occurred in a Southeast Asian community. Symptoms included high fever, chills, headache, and a cough or breathing difficulty. Avirus with the structure shown in below figure was implicated as the cause of the infections. Which of the viruses listed below caused this outbreak?

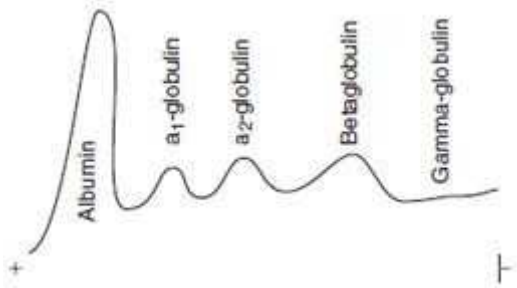


A. arenavirus
B. filovirus
C. poxvirus
D. rabies virus
E. SARS virus

Correct Answer: E
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
It has recently been shown that severe acute respiratory syndrome or SARS is caused by a corona- associated virus. This virus is a positive, single-stranded RNA, enveloped virion which has petal-like projections called corona, and is shown in below figure. The structure of rabies virus is bullet-shaped (choice D). Poxvirus is a very large, brick-shaped, very complex virus (choice C). Filovirus, such as the Ebola, or Marburg virus is very long and filamentous (choice B). Arenaviruses, like the lymphocytic choriomeningitis, or Lassa fever virus are circular, and have granules (arena) of nonfunctional ribosomes on their surfaces (choice A).

QUESTION 762
below figure depicts an electrophoretic pattern of serum proteins. This electrophoretic pattern is likely to be obtained from a 6-month-old infant suffering from recurrent pyogenic infections. He has which of the following diseases?



A. Addison disease
B. Bruton disease
C. Graves disease
D. Goodpasture syndrome
E. Myasthenia gravis

Correct Answer: B
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
Bruton disease is an X-linked congenital agammaglobulinemia. Thus, electrophoresis of the serum of infants, after the passively transferred maternal antibodies have been eliminated, reveals the absence or very low levels of gamma globulin. In contrast to Bruton disease all the other diseases listed will reveal a gamma globulin peak. Goodpasture syndrome (choice C) and Addison disease (choice A) are caused by autoantibody production to basement membrane of kidney and adrenal cortex, respectively. Myasthenia gravis (choice E) involves autoantibody production to acetylcholine receptor of the neuromuscular junctions. Graves disease (choice D) is caused by autoantibody production to thyroid- stimulating hormone receptors.

QUESTION 763
A 20-year-old prostitute presents at a local clinic with fever and abdominal tenderness at day 2 of her menstrual cycle. Gram-negative diplococci are seen in a Gram stain of vaginal secretions with many of the bacteria inside PMNs. Which of the following is likely the most important virulence factor necessary for this organism to initiate infection?

A. capsule
B. endotoxin
C. hyaluronidase
D. pili
E. protease

Correct Answer: D
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
The most important presumptive diagnostic test for gonorrhea is the demonstration of gram-negative, kidney-shaped diplococcic inside PMNs obtained from thick, creamy urethral exudates. Outside the human host, N. gonorrhoeae is fragile and usually do not survive well and are rapidly killed by drying, heat, and many disinfectants. Inside the host, however, the cocci possess virulence factors that enhance the organism's ability to establish mucus membrane infections. Pili (choice D) are hair-like appendages that extend out several micrometers. They enhance attachment to host cells and resistance to phagocytosis and are the most significant virulence factor. Polysaccharide capsules (choice A) do not appear to be as significant for gonococci infection as they do for N. meningitides infections. N. gonorrhoeae endotoxin (choice B) or LPS is a significant factor for toxicity once infection is established. A protease (choice E) can split IgA molecules, inactivating those antibodies, as do the meningococci. Hyaluronidase (choice D) can be an important virulence factor for grampositive cocci.

QUESTION 764
Which of the following approaches is likely to prevent future infection of patrons of the sex worker in question 24?

A. frequent washing of the genital area
B. immunization with the appropriate toxoid
C. prophylactic use of 100 units oral penicillin
D. use of condoms
E. vaccination with heat-killed germs

Correct Answer: D
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
Prevention of gonorrhea rests on the use of safe, properly worn condoms, and immediate treatment of symptomatic patients as well as their sexual partners. Ceftriaxone is the best treatment for uncomplicated cases of gonococcal infections. Since 1976, penicillinase-producing strains of N. gonorrhoeae have been isolated that show a high level of resistance to penicillin. Thus, use of 100 units of penicillin will be of little if any value for the prevention of gonorrhea (choice C). There are no vaccines composed of either killed germs (choice E) or toxoids (choice B) available for the prevention of gonorrhea. Frequent washing of the genital areas is not likely to prevent gonorrhea (choice A).

QUESTION 765
Aboy picked up a grounded bat and was bitten on the hand, suffering a slight wound. In addition to flushing the wound, cleaning it surgically, and giving antitetanus prophylaxis and antibiotics as indicated, the physician should immediately perform which of the following?

A. observe the boy very carefully
B. order a search for the attacking bat for autopsy
C. report the incident to the state epidemiologist
D. start rabies vaccine
E. start rabies vaccine and give antirabies serum

Correct Answer: E
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
If exposure to rabies virus appears definite, as in this case, treatment with human diploid cell live- derived vaccine and hyperimmune antirabies gamma globulin should be started immediately. Serum antibodies provide an immediate barrier to the growth of virus; meanwhile, antibodies are elicited by the vaccine. If the level of exposure is minimal (e.g., no skin puncture) and the animal probably is not rabid, vaccine is not recommended. Ordering a search for the attacking fox for autopsy to determine if it has rabies is like searching for a needle in a haystack, and thus not the best approach to address a possible rabies infection, which requires immediate actions (choice B). Initiation of rabies vaccine will lead to production of antibodies against the rabies virus, but it will require approximately 2 weeks to develop protective antibodies. By that time, severe damage may have already occurred (choice D). Postexposure immunization and human rabies immunoglobulin is the best approach. Observation of the patient (choice A) or reporting of the incident to the state epidemiologist (choice C) do not address the real needs of an individual running the risk of rabies.

QUESTION 766
A 60-year-old male with a chronic cough, bloody sputum, and marked weight loss is diagnosed as having tuberculosis. A "serpentine-like" colonial morphology is noted on Lowenstein- Jensen agar. This latter finding is due to which of the following factors?

A. coagulase
B. endotoxin
C. large "slimy" capsule
D. trehalose-6,6'-dimycolate
E. Wax D

Correct Answer: D
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
Mycobacteria are rich in lipids. These include mycolic acids, waxes, and phosphatides. In the cell, the lipids are largely bound to proteins and polysaccharides and are, to some extent, responsible for acid- fastness. Virulent strains of tubercle bacilli form microscopic "serpentine cords" in which acid-fast bacilli are arranged in

parallel chains. Cord formation is correlated with virulence and a "cord factor" (trehalose-6, 6-dimycolate choice D) has been extracted from virulent bacilli. It inhibits leukocyte migration, causes chronic granulomas, and may serve as an immulogical adjuvant. Virulent mycobacteria do not have endotoxin (choice B) as do the enteric bacteria which may cause inflammation. Nor do mycobacteria produce coagulase (choice A). Mycobacteria colonies are usually rough and dry, not "slimy" from a capsule (choice C). Wax D (choice D) is present in mycobacteria, but is not associated with cord factor.

QUESTION 767
Darrin is an intern working in the emergency room at the local county hospital. Mr Arnold, a 48-year- old homeless man, comes in complaining of "feeling real bad." Mr Arnold's mentation is altered, and is unable to verbalize his past medical history. Darrin is having difficulty examining the patient because his body emits a tremendous odor. While examining him, Darrin discovers that his right leg is red, swollen, sore, and covered with ulcers. The nurse in the emergency room covers the leg with dressings and a plastic bag to contain the smell. By morning, Mr Arnold's anaerobic blood cultures become positive with grampositive rods. Darrin observes that the bag is full of air, and when he removes it the smell is overwhelming. What should Darrin do?

A. Arrange for Mr Arnold to receive hyperbaric oxygen therapy.
B. Consult with a surgeon, as Mr Arnold will need debridement and IV antibiotics.
C. Continue the broad spectrum IV antibiotics he has prescribed for Mr Arnold.
D. Put Mr Arnold in respiratory isolation and confirm his diagnosis with a spinal tap.

Correct Answer: B
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
Darren's patient is most likely suffering from an infection that is caused by toxin-producing clostridia. C. perfringens and related clostridia can produce invasive infection (myonecrosis and gas gangrene) if they are introduced into damaged tissue. These organisms produce a large variety of toxins that may be lethal, necrotizing, and/or hemolytic. Clostridia are anerobic bacteria and can only grow well in conditions of low oxygen contact, such as necrotic tissue. In such an infection, within a few days there is foul-smelling discharge, fever, hemolysis, toxemia, shock, and death. Treatment includes immediate surgery and antibiotic administration. Hence, choice B would be the next appropriate medical intervention. Hyperbaric oxygen (choice A) has no proved effect in this situation. Antibiotics only (choice C) would provide only partial resolution and not in a timely manner. Choice D has nothing to do with the medical management of Darren's patient.

QUESTION 768
Which of the following chemical agents is a powerful oxidizing agent used to kill microorganisms?

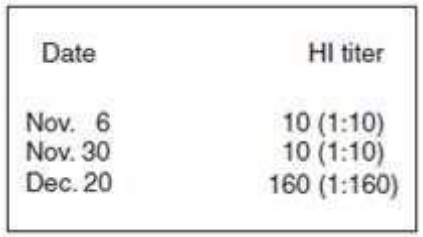
A. benzoic acid
B. chlorine
C. ethyl alcohol
D. ethylene oxide
E. mercury

Correct Answer: B

Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
Chlorine (choice B) is a halogen that is often used for microbial disinfection and antisepsis. Many compounds can release various forms of chlorine (OCl-, HOCl, Cl2) that can kill microorganisms by oxidation. These include sodium hypochlorite, chlorine dioxide, and sodium dichlaroisocyanrate, oxidizing agents that destroy the cellular activity of proteins. Hypochlorous acid is the active ingredient for bactericidal and viruscidal effects. Such compounds may be sporocidal. Iodine (I2) may also be bactericidal, fungicidal, tuberculocidal, viruscidal, and sporocidal. Mercury (choice E) is antimicrobial but dangerous to humans. Ethanol (choice C) has limited killing ability for bacteria. Benzoic acid (choice A) has limited antimicrobial use, which ethylene oxide (choice D) is able to sterilize (completely kill all organisms) materials, but is very dangerous to humans as well.

QUESTION 769
On November 6, a patient had the onset of an illness characterized by fever, chills, headache, cough, and chest pain. The illness lasted 1 week. On December 5, she had another illness very similar to the first, which lasted 6 days. She had no flu immunization during this period. Her Hl titer to swine flu virus is shown in below figure. (There were no laboratory errors in any of the tests.) Which of the following is the most valid conclusion?



Date	HI titer
Nov. 6	10 (1:10)
Nov. 30	10 (1:10)
Dec. 20	160 (1:160)

A. It is impossible to relate either illness with the specific virus.
B. The patient was ill with swine flu later, and the November 6 illness was due to another pathogen.
C. The patient was ill with swine flu on December 20.
D. The patient was ill with swine flu on November 6.

Correct Answer: B
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
Influenza viruses are classified into three main groups (A, B, and C) based on proteins in the ribonucleoprotein capsid. Each virus can be further subdivided into various groups when the hemeagglutinin (HA) and NA glycoproteins are examined. So far, 15 subtypes of HA (H1H15) and 9 subtypes of NA have been identified, and these can be found in many different combinations for influenza virus types or strains. Influenza viruses also have the ability to attach to and to agglutinate various types of red blood cells, including chicken RBCs. Antibodies made against HA antigens will neutralize HA activity and inhibit HA. This HI data can be used

clinically to determine whether the same or different flu viruses have caused single or multiple outbreaks. In our clinical episode in this question and below figure, an HI titer of 10 (or 1:10 dilution of the patient's serum) represents little or no specific antibody against the specific virus, (swine flue virus) used in the HI test. Infection may have occurred in the past, with only small amounts of specific antibody remaining. The 160 (1:160) titer indicates a large amount of specific anti-swine flu immunoglobulins are now present. Apositive diagnosis for swine flu infection by December 20 is stated because it is fourfold or higher than the November 30 serum sample. As a result, choice B is the proper interpretation of these serological test results. Choice A is incorrect because we have specifically measured antibodies against swine flu on December 20. Choice C is partially correct but does not interpret results for November 6 and 30. Choice D is specifically incorrect since only swine flu was used in this HI test and the November 6 data is essentially negative.

QUESTION 770
Viruses have various ways of entering the human body and producing disease. Which of the following descriptions accurately describe the route and mechanism for the virus indicated?

A. Coronaviruses enter the gastrointestinal tract through the mouth and move into the stomach, where they proliferate within mucosal cells to produce peptic ulcers.
B. Enteroviruses enter through the mouth, replicate in the pharynx and bowel, and move via the blood to distant target organs (central nervous system).
C. HIV is directly injected into the blood stream by insects requiring blood for egg development.
D. Influenza viruses enter through the respiratory tract, replicate within lymphocytes in the lung, and move via the lymphatic vessels to joints and the central nervous system to produce muscle aches, stiff joints, and fever.
E. Mumps virus enters through abraded skin in the genital area and moves into the testicles of males to produce swelling and sterility.

Correct Answer: B
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
It is important that physicians have a good understanding of how pathogens, including viruses, enter into the human host and know what symptoms may be caused by the microorganism. Such knowledge and interpretations may have significant value in making a meaningful differential diagnosis. Enteroviruses do enter through the mouth, replicate in the pharynx and bowel before using the blood system (viremia) to access final target organs (choice B). Coronaviruses (choice A) are inhaled or ingested (small number of strains), but do not produce peptic ulcers. Insects have been shown to not be important for HIV transmission (choice C). Influenza viruses (choice D) do not replicate in lung lymphocytes. Mumps virus (choice E) is most often inhaled from respiratory secretions from infected individuals who make large numbers of the viruses in the upper respiratory tract during the prodromal period.

QUESTION 771
What would be the appearance of invasives C. albicans in a Gram-stained abnormal vaginal smear?

A. arthrospores-alternating filled and empty
B. branching mycelia
C. budding yeast cells and hyphae
D. endosporulating spherules

E. single yeast cells

Correct Answer: C
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
Candida species are considered to be opportunistic microorganisms. They are normal or usual members of the skin, mucus membranes, and the GI tract. The risk of endogenous opportunistic infection is ever- present. In culture or tissue, candida species grow as oval, budding yeast cells (36 m) which stain blue in the Gram-stain procedure. They also form pseudohyphae when the buds grow, but fail to detach. C. albicans is dimorphic, being also able to produce true hyphae. Diagnostically, C. albicans will begin to form true hyphae (germ tubes) in serum at 37℃ in the labora tory. With these characteristics in mind, choice C is correct. Alternating filled and empty arthrospores (choice A) is characteristic of coccidioides. Branching mycelia (choice B) is a general characteristic seen in any mold colony on agar and is not specific for candida. Endosporulating spherules (choice D) are also seen in tissue with coccidioides. Single yeast cells (choice E) may be occasionally seen with candida, but most candida spores will be associated with buds and pseudohyphae.

QUESTION 772
The tetracycline antimicrobials are effective specifically in prokaryotes due to which of the following activities?

A. They are transported into prokaryotes but not into eukaryotes.
B. They bind to prokaryotic and not eukaryotic DNA-directed RNA polymerase.
C. They bind to prokaryotic but not eukaryotic membranes.
D. They bind to prokaryotic but not eukaryotic aminoacyl-tRNAs.
E. They inhibit prokaryotic protein synthesis initiation, which specifically requires formylmethionyl tRNA.

Correct Answer: A
Section: Microbiology/Immunology
Explanation

Explanation/Reference:
Explanation:
The specificity of the tetracycline antibiotics is attributable to an energy-dependent transport system present in prokaryotes, but not in eukaryotic cells. This transport system results in accumulation of the drug inside the bacterial cell, where it binds to the ribosome and interferes with binding of aminoacyl tRNA to the acceptor site. Tetracyclines bind to the bacterial ribosome, but not to DNA-directed RNA polymerase, or prokaryotic membranes (choices B and C). Tetracyclines do not inhibit initiation of protein synthesis, which specifically requires formylmethionyl tRNA (choice E). Both prokaryotic and eukaryotic cells bind tetracyclines. However, the prokaryotic cells have much more effective tetracycline transport systems than eukaryotic cells. Thus, prokaryotic cells accumulate higher intracellular concentrations of tetracyclines than eukaryotic cells, which induce a significant inhibition of protein synthesis only in prokaryote cells (choice D).

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