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QUESTION 1

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 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-1phosphate 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 Nacetylglucosamine 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 2

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 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 3

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?

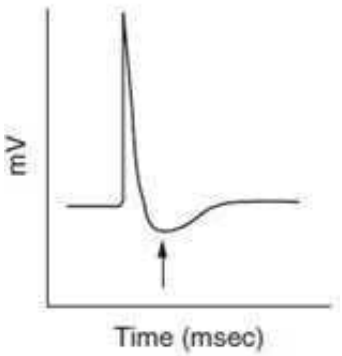


FIG. 2-24

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 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 4

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

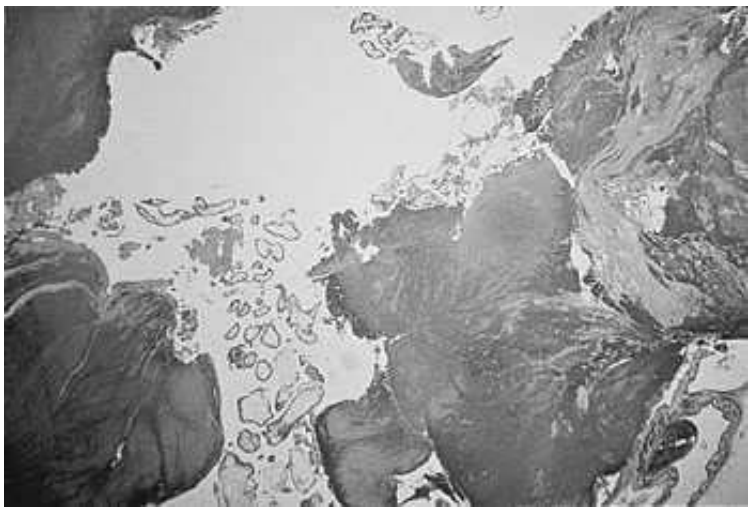
E. skeletal muscle

Correct Answer: D

Section: Physiology 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 5

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 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 6

A 3-year-old child with a history of recurrent staphylococcal infections arrives at the emergency department at the local hospital. His neutrophils show normal chemotaxis, degranulation, and phagocytosis. However, intracellular killing of staphylococci by the neutrophils is severely impaired. Myeloperoxidase activity of his neutrophils is normal. The child has no history of streptococcal infection. Which of the following is the most likely disease affecting this patient?

A. chronic granulomatous disease

B. Graves disease

C. rheumatoid arthritis

D. severe combined immunodeficiency disease (SCID)

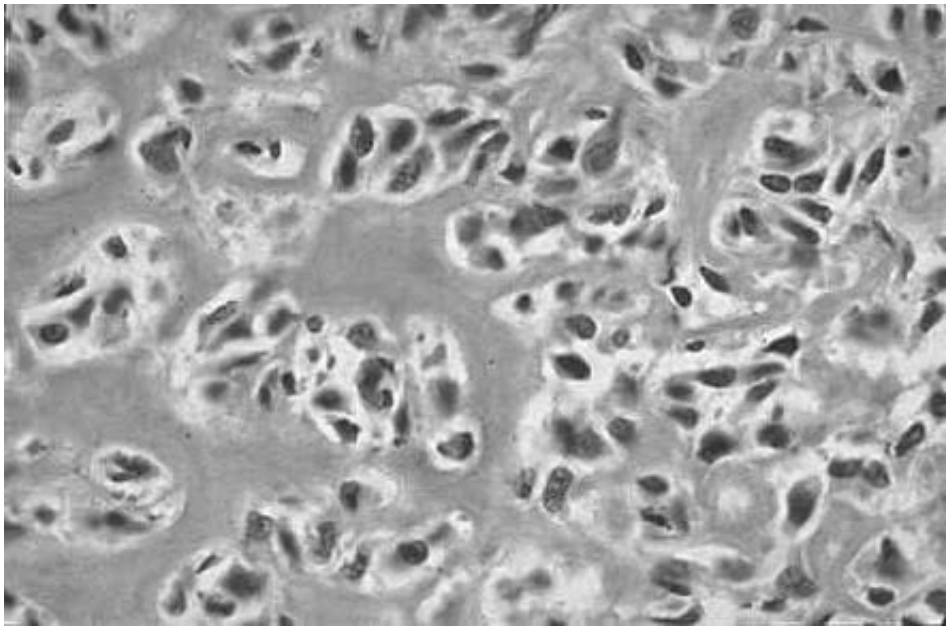
E. systemic lupus erythematosus (SLE)

Correct Answer: A

Section: Microbiology/Immunology This patient has chronic granulomatous disease. Children with this disease suffer chronic suppurative infections caused most frequently by S. aureus. The cause of chronic granulomatous disease is most commonly an X-linked disorder related to a genetic defect in NADPH oxidase, leading to a deficiency of NADPH oxidase. Neutrophils contain myeloperoxidase, which utilizes hydrogen peroxideand halide ions to produce hypochlorite, which is highly microbicidal. Because of the defective NADPH oxidase, the patient\\'s phagocytes cannot generate sufficient hydrogen peroxide, thus the myeloperoxidase- hydrogen peroxide-halide system cannot function normally. Neutrophils from these patients can phagocytize bacteria and fungi normally, but they cannot kill them because of the defective myeloperoxidase-hydrogen peroxide-halide system. Also, laboratory analysis reveals an absent respiratory burst as demonstrated by a negative nitroblue tetrazolium test in patients with chronic granulomatous disease Severe combined immunodeficiency disease (SCID) is characterized by the absence of T and B cells, absence of thymus, and a lack of lymphocyte proliferative response to mitogens, antigens, and allogeneic cells in vitro (choice D). Systemic lupus erythematosus is an autoimmune disease (type III hypersensitivity or immune-complex disease). Patients with lupus erythematosus produce anti-DNA antibodies (choice E). Rheumatoid arthritis is another autoimmune disease. Patients with this disease produce IgM autoantibodies to the Fc moiety of IgG (choice C). Patients with Graves disease produce autoantibodies to thyroid-stimulating hormone receptors (choice B).

QUESTION 7

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 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 8

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 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 9

Exhibit #1:

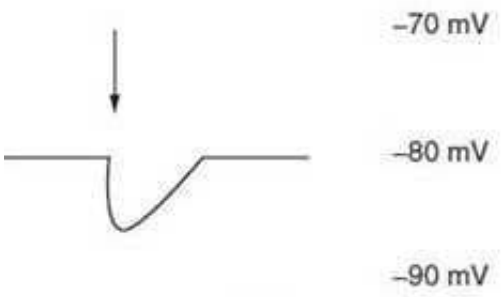


FIG. 2-23

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

QUESTION 10

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 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 11

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

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 12

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 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 13

Naloxone would be contraindicated in an apparently psychotic patient if one were to also discover which of the following?

A. The patient had a psilocybin-induced psychosis.

B. The patient has hypertension.

C. The patient has just suffered a fracture.

D. The patient is a placebo responder.

E. The patient is an alcohol abuser.

Correct Answer: C

Section: Behavioral Science and Biostatics Naloxone is an opiate antagonist, and would be contraindicated in a patient with fracture who would require rapid pain relief. The placebo analgesic effect seems to be endorphin mediated, and naloxone would block it. The other choices do not deal with naloxone\\'s specific anti-opioid activity.

QUESTION 14

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 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 15

A 60-year-old woman is admitted to the hospital with a fever and severe diarrhea for the last 24 hours. Cultures of blood, cerebrospinal fluid, urine, and stool are all negative for pathogens. The profile of gut hormones reveals elevated levels of VIP. An analogue of which of the following would most likely lower her VIP levels?

A. erythromycin

B. histamine

C. motilin

D. somatostatin

E. trypsin

Correct Answer: D

Section: Physiology VIP is a neurotransmitter in the brain and in the parasympathetic nerves of the digestive tract. It also acts as a hormone. VIP has a secretin-like effect on the pancreas. It increases the volume of water and bicarbonate output and affects GI blood flow and motility. All this contributes to severe secretory diarrhea in the case of VIP overproduction. Somatostatin is the best choice because it has a broad range of inhibitory effects, inhibiting GI secretions, slowing GI motility, and reducing splanchnic blood flow. An analogue of somatostatin, called octreotide, was found useful for treatment of syndromes related with VIP overproduction. Octreotide has a longer half-life than physiologic somatostatin. Erythromycin (choice A) is known to have antibiotic features. This is not the best choice, since no pathogens were found. Histamine (choice B) is a physiologic stimulant of gastric hydrochloric acid secretion, potentiating the effects of acetylcholine and gastrin. Motilin (choice C) stimulates gastric motility, which is contraindicated for diarrhea. Trypsin (choice E) is a protease released by pancreatic cells, breaking peptide bonds as well as converting many other proteolytic enzymes to their active form. All of the negative choices will not affect, and in fact may even worsen the VIPrelated symptoms.