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QUESTION 1

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 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 2

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. aeruginosa
- E. Y. pseudotuberoulis

Correct Answer: C

Section: Microbiology/Immunology

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. pseudotuberculosis (choice E) resides in domestic farm animals and is the source of human

infections.

QUESTION 3

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 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 A and D). Treatment with compatible B or T cells may provide very brief humoral or cellular immunity (choices B and E).

QUESTION 4

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

- A. both are increased
- B. both are decreased
- C. neither is different from at rest
- D. sympathetic activity to the heart is decreased while that to the cutaneous vasculature is increased
- E. sympathetic activity to the heart is increased while that to the cutaneous vasculature is decreased

Correct Answer: E

Section: Physiology 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 5

I-cell disease (also identified as mucopolipidosis 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 N-acetylglucosamine-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 N-acetylglucosamine phosphotransferase yielding N-acetylglucosamine-1-phosphate-6-mannoseprotein. A second reaction removes the N-acetylglucosamine leaving mannose residues phosphorylated in the sixth position. A specific 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 (mucopolipidosis II) and pseudo-Hurler polydystrophy (mucopolipidosis 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.

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