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QUESTION 1

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 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 2

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. A complement 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 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 3

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 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 4

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 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 the action of cyclooxygenases. NSAIDs do not regulate bradykinin and histamine synthesis (choices B and D).

QUESTION 5

A retired policeman who received a kidney transplant developed a generalized infection by an enveloped double-stranded DNA virus. This organism formed owl's eye inclusions in cells found in urinary sediments. Which of the following viruses is the most likely etiological agent? Which of the following approaches most likely might have prevented the infection of the policeman?

- A. administration of gamma interferon
- B. injection of alpha interferon
- C. treatment with methisazone
- D. treatment with zanamivir
- E. viral screening of donor and recipient

Correct Answer: E

Section: Microbiology/Immunology In this case, prevention of infection most likely involves careful prescreening of the kidney donor and the recipient for CMV presence by antibody detection, isolation, or PCR. For treatment, ganciclovir is moderately effective for CMV pneumonia and retinitis in AIDS patients. Alpha interferon is used for patients with chronic hepatitis caused by B or C virus. However, only some genotypes appear to be susceptible (choice B). Gamma interferon, like alpha, has been shown to have viral replicative inhibitory activity, and also to be able to activate macrophages as well as other immune cells (choice A). Zanamivir inhibits the release of influenza virus from infected cells and thus limits the infection (choice D). Methisazone inhibits protein synthesis of vaccinia and smallpox viruses (choice C).

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