FOCUS: HUMAN IMMUNODEFICIENCY VIRUS

Continuing Education Questions

FALL 2006

To receive 2.0 contact hours of intermediate level P.A.C.E.[®] credit for the Focus: Human Immunodeficiency Virus questions, insert your answers in the appropriate spots on the continuing education registration form that follows, then mail a photocopy of the form as directed.

LEARNING OBJECTIVES

- 1. Describe the main genetic properties of the human immunodeficiency virus (HIV).
- 2. Describe the major events in the life cycle of HIV.
- 3. Identify the primary functions of each of the following viral proteins: gp120, gp41, reverse transcriptase, integrase, protease.
- 4. List the three major stages in the natural course of the HIV infection.
- 5. Describe the changes in the viral loads and the CD4 counts during the natural course of the HIV disease.
- 6. List the four FDA-approved classes of antiretroviral drugs and identify the molecular targets of therapy for each class.
- 7. Describe benefits and limitations of antiretroviral therapy.
- 8. Describe the mechanisms of resistance in each of the four FDA-approved classes of antiretroviral drugs.
- 9. List the two fundamental approaches to HIV drug resistance testing.
- 10. Describe the principles of phenotypic resistance testing and list the main steps of the testing process.
- 11. Define IC50 and calculate the X-fold reduction in susceptibility using the IC50 values.
- 12. Describe the principles of sequencing-based genotypic resistance testing and list the main steps of the testing process.
- 13. Describe the principles of dideoxynucleotide sequencing.
- 14. Describe the principles and the limitations of hybridization-based resistance assays.
- 15. Discuss the clinical utility of HIV drug resistance testing.

CONTINUING EDUCATION QUESTIONS

- 1. Which of the following is an accurate description of the genetic properties of HIV?
 - a. HIV is an RNA virus capable of converting its genetic material to DNA.
 - b. HIV is a DNA virus with high affinity for endothelial cells and B-lymphocytes.

- c. HIV is an RNA virus with extremely stable and conserved genome of 500 kilobases.
- d. HIV is a DNA virus replicating with an error rate of 0.1 mistake per base per replication cycle.
- 2. Viral enzymes reverse transcriptase, protease, and integrase are transcribed from which of the following genes?
 - a. Gag
 - b. Pol
 - c. Env
 - d. Rev
- 3. During the life cycle of HIV, the gp160 precursor protein is cleaved to form:
 - a. p24, p17, gp118.
 - b. gp60 and p100.
 - c. gp90 and p70.
 - d. gp120 and gp41.
- 4. The primary role of the protease in the life cycle of HIV is to:
 - a. integrate the provirus into the host genome.
 - b. interact with the CD4 receptor initiating the membrane fusion.
 - c. form the functional proteins of HIV by cleaving the inactive precursors.
 - d. regulate the transcription of the HIV genes.
- 5. The three main stages in the natural course of the HIV disease are:
 - a. reverse transcription, clinical latency, AIDS.
 - b. reverse transcription, transcriptional latency, AIDS.
 - c. acute infection, clinical latency, AIDS.
 - d. acute infection, membrane fusion, AIDS.
- 6. Which of the following laboratory findings would lead to the diagnosis of AIDS according to the CDC criteria?
 - a. CD4 count 150 cells/µL, viral load 5,000,000 copies/mL
 - b. CD4 count 280 cells/µL, viral load 10,000,000 copies/mL
 - c. CD4 count 350 cells/µL, viral load 500,000 copies/mL
 - d. CD4 count 800 cells/µL, viral load 100 copies/mL

- 7. The four FDA-approved classes of antiretroviral drugs are:
 - a. nucleoside analogue reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), RNA polymerase inhibitors, integrase inhibitors.
 - b. nucleoside analogue reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), protease inhibitors, fusion inhibitors.
 - c. nucleoside analogue reverse transcriptase inhibitors (NRTIs), gp120 inhibitors, protease inhibitors, acetylcholinesterase inhibitors.
 - d. nucleoside analogue reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), protease inhibitors, neuraminidase inhibitors.
- 8. Which of the following viral proteins is the primary target for the cytidine analogues, lamivudine, zalcitabine, and emtricitabine?
 - a. Reverse transcriptase
 - b. Protease
 - c. Integrase
 - d. Gp41
- 9. All of the following are benefits of highly active antiretroviral therapy (HAART), EXCEPT:
 - a. lower viral loads.
 - b. higher CD4 counts.
 - c. reversed or delayed progression to AIDS.
 - d. absence of serious side effects and long term toxicities.
- 10. The two main biochemical mechanisms leading to NRTI (nucleoside analogue reverse transcriptase inhibitor) resistance are:
 - a. sterical inhibition and primer unblocking.
 - b. sterical inhibition and ritonavir boosting.
 - c. primer unblocking and substitutions in the HR1 domain of gp41.
 - d. substrate cleft and flap region substitutions in the protease.
- 11. K103N mutation is primarily associated with resistance to:
 - a. nucleoside analogue reverse transcriptase inhibitors.
 - b. non-nucleoside reverse transcriptase inhibitors.
 - c. protease inhibitors.
 - d. integrase inhibitors.

- 12. The two fundamental approaches to HIV drug resistance testing are:
 - a. genotypic testing and Western Blot.
 - b. genotypic testing and karyotyping.
 - c. genotypic testing and phenotypic testing.
 - d. phenotypic testing and Western Blot.
- 13. HIV RNA extraction, reverse transcription, amplification, recombinant vector preparation, and quantitative assessment of viral replication in cell culture are steps of:
 - a. genotypic resistance testing.
 - b. phenotypic resistance testing.
 - c. resistance testing by reverse hybridization.
 - d. resistance testing by karyotyping.
- 14. IC50 may be defined as:

a. the concentration of the drug that results in a 50% inhibition of viral growth.

b. the concentration of the drug that results in a 50% increase in the CD4 counts.

- c. the concentration of the drug that reduces the chance of progression to AIDS within one year by 50%.
- d. the concentration of the drug that reduces the incidence of primary resistance mutations by 50%.
- 15. If the IC50 of the wild-type virus is 2 mg/mL and the IC50 of the patient's isolate is 6 mg/mL, then the X-fold reduction in susceptibility will be reported as:
 - a. 3-fold resistance.
 - b. 4-fold resistance.
 - c. 8-fold resistance.
 - d. 12-fold resistance.
- 16. HIV RNA extraction, reverse transcription, amplification, dideoxynucleotide sequencing, and algorithmic interpretation of the sequencing data are steps of:
 - a. phenotypic resistance testing.
 - b. genotypic resistance testing.
 - c. resistance testing by karyotyping.
 - d. resistance testing by Western Blot.
- 17. A double peak appears on the electrophoretogram during the process of dideoxynucleotide sequencing when:
 - a. a mixture of two nucleotides is detected at a specific position.
 - b. a single wild-type nucleotide is detected at position 103 of reverse transcriptase.
 - c. the M184V mutation is detected in the patient's isolate.

- d. a single nucleotide substitution is detected at a resistance-associated position in the protease.
- 18. During the process of dideoxynucleotide sequencing, which of the following procedures is used to arrange the DNA strands in the order of increasing length?
 - a. Radial immunodiffusion
 - b. Polyacrylamide gel electrophoresis
 - c. Reverse transcriptase polymerase chain reaction (RT-PCR)
 - d. Western Blot
- 19. Resistance testing by reverse hybridization involves:
 - a. synthesis of new DNA strands complementary to the target sequence of interest in the presence of labeled chain terminators.
 - b. determination of IC50 for the patient's isolate and the wild-type virus.

- c. binding of the amplified biotinylated DNA material to codon-specific oligonucleotide probes.
- d. preparation of RT-PR deficient vectors.
- 20. The clinical utility of HIV drug resistance testing has been evaluated in a number of studies with the following results (select the correct answer).
 - a. All studies demonstrated the benefit of resistance testing.
 - b. All studies failed to demonstrate the benefit of resistance testing.
 - c. Some studies demonstrated the benefit of resistance testing while other studies failed to demonstrate the benefit of resistance testing.
 - d. All studies demonstrated the benefit of phenotypic resistance testing but failed to demonstrate the benefit of genotypic resistance testing.

Clinical Laboratory Science Announces 2005 Distinguished Author Award Recipients

Recipients of the *Clinical Laboratory Science* Distinguished Author Awards are chosen by *Clinical Laboratory Science* editorial board members. Nominations are based upon based on originality and quality of writing, relevance to the laboratory science profession, and integration of theory and application. The editorial board of *Clinical Laboratory Science* is pleased to announce the following recipients of the 2005 Distinguished Author Awards.

Clinical Practice

Bobbi Dock, for her article *Improving the Accuracy of Specimen Labeling*, published in the Fall 2005 issue of *Clinical Laboratory Science*.

Research and Reports

Heidi Andersen, for her article *Children on the Frontline against E.coli: Typical Hemolytic-Uremic Syndrome*, published in the Spring 2005 issue of *Clinical Laboratory Science*.

Focus

Tim R Randolph, for his article *Chronic Myelocytic Leukemia - Part I: History, Clinical Presentation, and Molecular Biology*, published in the Winter 2005 issue of *Clinical Laboratory Science*.

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Participant Information

Please circle the most appropriate answers.

1. Is this program used to meet your CE requirements for: (a) state license (b) NCA (c) employment (d) other

2. Did these articles achieve their stated objectives?(a) yes (b) no

3. How long did it take you to complete both the reading and the quiz? ______minutes

4. What subjects would you like to see addressed in future Focus articles?



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