

JMD CME Program in Molecular Diagnostics 2008

American Society for Investigative Pathology *and the*
Association for Molecular Pathology

The Journal of Molecular Diagnostics, Volume 10, No. 4 (July 2008)

<http://jmd.amjpathol.org>

www.asip.org/CME/jmdCME.htm

www.amp.org/CME/jmdCME.htm

Mark E. Sobel, MD, PhD, Director of Journal CME Programs

CME Questions # 27-34

(See January-May 2008 Examination Sheets for Questions # 1-26)

27. Epstein-Barr virus (EBV) causes infectious mononucleosis and is also associated with a wide variety of malignancies and disorders. Based on the referenced Review, select the ONE statement that is NOT true: [See J Mol Diagn 2008 10:279-292; no authors of the referenced article disclosed any potential conflicts of interest.]

- The prevalence of EBV-related cancers is estimated to affect up to 1% of the world's population.
- High-risk individuals may benefit from screening tests that predict impending progression so that preemptive measures may be taken even before disease is clinically evident.
- EBV infects up to 10% of the adult population.
- Healthy carriers seem to harbor EBV almost exclusively in B lymphocytes.
- In healthy carriers, cell-free body fluids such as serum or plasma contain negligible amounts of EBV DNA.

28. EBV is capable of infecting a wide spectrum of cell types. Based on the referenced Review, select the ONE statement that is NOT true: [See J Mol Diagn 2008 10:279-292; no authors of the referenced article disclosed any potential conflicts of interest.]

- EBV is capable of infecting B lymphocytes, squamous and glandular epithelial cells, myoepithelial cells, smooth muscle cells, T cells, NK cells, plasma cells, and follicular dendritic cells.
- Children with Bruton's agammaglobulinemia are particularly susceptible to infection with EBV and harbor a very high viral load in their B lymphocytes compared to most patients with infectious mononucleosis.
- When a cell is infected with EBV, the double-stranded viral DNA circularizes to form an episome that may then replicate to produce 1 to 50 clonal copies of the EBV genome.
- The number of tandem repeat sequences found at the ends of the EBV genome varies from virion to virion.
- Latent infection is characterized by limited expression of viral proteins, such as EBV nuclear antigen 1 (EBNA1), which avoids immune recognition and destruction.

29. Serologic tests are often used to confirm infection and document remote infection. Based on the referenced Review, select the ONE statement that is NOT true: [See J Mol Diagn 2008 10:279-292; no authors of the referenced article disclosed any potential conflicts of interest.]

- The heterophile antibody test (colloquially called the "Monospot" test) is no longer widely used to diagnose patients with infectious mononucleosis-like symptoms.
- Mononucleosis-like symptoms include fever, sore throat, lymphadenopathy, hepatosplenomegaly, malaise, and headache.
- EBV-related cancer is typically associated with high serologic titers against early antigen (EA) and IgG viral capsid antigen (VCA) with low EBNA titer.
- Serology is not reliable when the immune system is dysfunctional, such as in AIDS or allogeneic transplant patients.
- Nasopharyngeal cancer patients often have high IgA titers against lytic EBV proteins.

30. EBV-encoded RNAs (EBERs) are reliably expressed in virtually all latently infected cells in both benign and malignant lesions. Based on the referenced Review, select the ONE statement that is NOT true: [See J Mol Diagn 2008 10:279-292; no authors of the referenced article disclosed any potential conflicts of interest.]

- a. *EBER in situ* hybridization is the assay of choice in clinical laboratories for defining a lesion as EBV-related.
- b. *EBER1* and *EBER2* are non-polyadenylated RNA transcripts that are abundantly expressed in latently infected cells.
- c. Oral hairy leukoplakia is an exceptional lesion in which *EBER* is downregulated.
- d. Nearly all keratinizing nasopharyngeal carcinomas are EBV-related as demonstrated by *EBER in situ* hybridization.
- e. In Western nations, anaplastic large cell lymphoma is virtually never *EBER*-positive.

31. Automation is becoming important to improve efficiency and standardization in the clinical laboratory. Based on the referenced Technical Advances article that compares automated nucleic acid extraction methods with manual extraction, select the ONE statement that is NOT true: [See J Mol Diagn 2008 10:311-316; no authors of the referenced article disclosed any potential conflicts of interest.]

- a. Three extraction methods were evaluated for their ability to afford nucleic acid for optimal polymerase chain reaction (PCR) amplification.
- b. The easyMAG system (bioMerieux, Durham, North Carolina) was found to be a user-friendly instrument, requiring 280 total steps to produce nucleic acid from 15 samples, compared to 534 for the manual extraction.
- c. Both the EZ1 (Qiagen, Valencia, California) and easyMAG systems considerably decreased hands-on-time compared to the manual method of extraction, saving between 29 and 47 minutes per batch, depending on the method.
- d. The setup of the easyMAG system does not change greatly when extracting specimens of different matrices and targets, while the EZ1 uses different program cards and reagent kits depending on target and matrix.
- e. Including reagents, disposables, and technical time to determine the cost of extraction, the easyMAG system is the least expensive of the extraction methods.

32. Sensitive detection of tumor-specific point mutations is of interest in both the early detection of cancer and the monitoring of treatment at a molecular level. Based on the referenced Technical Advances article, select the ONE statement that is NOT true: [See J Mol Diagn 2008 10:325-331; no authors of the referenced article disclosed any potential conflicts of interest.]

- a. Somatic mutations in the *K-ras* gene are present in at least 80% of pancreatic cancers and 35 to 50% of colorectal cancers.
- b. Peptide nucleic acid (PNA) is a synthetic DNA analogue in which the ribose/phosphate backbone of the DNA in PNA is replaced by N-(2-aminoethyl)-glycine units linked by peptide bonds.
- c. PNA oligomers bind so strongly to complementary DNA that one single mismatch in the PNA oligomer will not destabilize the complex between oligomer and DNA target.
- d. The sensitivity of PNA clamp PCR to detect *K-ras* mutations was limited by the low fidelity of Taq DNA polymerase.
- e. The sensitivity of the PNA clamp assay to detect *K-ras* mutations increased approximately 10-fold when Phusion HS DNA polymerase was used.

33. Cystic fibrosis (CF) is a common and serious condition with autosomal recessive inheritance. Based on the referenced article, select the ONE statement that is NOT true: [See J Mol Diagn 2008 10:368-375; no authors of the referenced article disclosed any potential conflicts of interest.]

- a. CF is caused by mutations in the cystic fibrosis transmembrane conductance regulator gene (*CFTR*) on chromosome 7q31.
- b. *CFTR* is primarily expressed in the apical membrane of exocrine epithelial cells.
- c. The CF phenotype is variable, ranging from mild with limited manifestations to severe with rapid deterioration and death within the first year of life.
- d. Large deletions and insertions are the most frequently reported sequence variants that have been reported to the Cystic Fibrosis Mutation Database.
- e. The range and frequency of individual *CFTR* mutations varies among different populations, ethnic backgrounds, and geographic locations.

34. In Hispanics, the CF mutation spectrum remains relatively poorly defined. Based on the referenced article, select the ONE statement that is NOT true: [See J Mol Diagn 2008 10:368-375; no authors of the referenced article disclosed any potential conflicts of interest.]

- a. The CF carrier frequency in Hispanics of ~1 in 3000 is significantly lower than that in Caucasians.
- b. Deletions involving exons 2-3, exons 17a-18, exon 20, exons 22-23, exons 22-24, and exon 24 have been described in Hispanic individuals.
- c. The 935delA mutation is a relatively common mutation in Hispanics.
- d. Small deletion mutations are especially likely to interfere with probe hybridization in multiplex ligation-dependent probe amplification (MLPA) analysis.
- e. Apparent exon deletions by MLPA may indicate the presence of both large deletions and point mutations.

Disclosures: No authors of the referenced articles disclosed any potential conflicts of interest.

SEE EXAMINATION ANSWER SHEET – NEXT PAGE

**TO REGISTER FOR THE JMD CME PROGRAM IN MOLECULAR DIAGNOSTICS:
www.asip.org/CME/jmdCME.htm or www.amp.org/CME/jmdCME.htm**

JMD CME Program in Molecular Diagnostics 2008

The Journal of Molecular Diagnostics, Volume 10, No. 4 (July 2008)

Mark E. Sobel, MD, PhD, Director of Journal CME Programs

<http://jmd.amjpathol.org>

www.asip.org/CME/jmdCME.htm

www.amp.org/CME/jmdCME.htm

CME Questions # 27-34

Examination Answer Sheet #4, Questions #27-34					
Answer	a	b	c	d	e
Question #27	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Question #28	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Question #29	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Question #30	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Question #31	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Question #32	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Question #33	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Question #34	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Name					
Email Address					
CME ID# (For office use only)					

Instructions for Completing and Submitting the Examination:

1. You must be registered for the JMD CME Program prior to submission or you may register along with submission of your first Examination Answer Sheet of the year. *
2. Fill in the appropriate circle for each question to indicate your answer.
3. Enter your name and email address.
4. Mail or fax this completed Examination Answer Sheet (along with your payment and CME Registration Form if you have not already registered*) to the ASIP CME office.
5. Keep a copy of your Examination Answer Sheet for your records to compare with correct answers.
6. Your score and correct answers will be emailed to you within 1 month.**

* Register online at www.asip.org/CME/journalCME.htm or you may submit your CME 2008 Registration Form with payment prior to, or along with, your first Examination Answer Sheet of the year. You may download the JMD CME Registration Form at www.asip.org/CME/jmdCME.htm or www.amp.org/CME/jmdCME.htm.

** You may mail or fax your completed Examination Answer Sheet from each issue of JMD in order to receive correct answers within 1 month, **OR** you may collect your completed Examination Answer Sheets throughout the year, and mail or fax to the ASIP CME office at the completion of the 2008 CME year.

Deadline for receipt of CME 2008 Registration Form, all Examination Answer Sheets, and CME Evaluation Form: January 15, 2009.

Complete Journal CME 2008 Information, including the CME Conflict of Interest Disclosure Policy, is on the ASIP and AMP websites at: www.asip.org/CME/jmdCME.htm and www.amp.org/CME/jmdCME.htm

Direct all Inquiries to:

ASIP CME Office
American Society for Investigative Pathology
9650 Rockville Pike
Bethesda, MD 20814-3993 (USA)
Tel: 301-634-7942; Fax: 301-634-7990
Email: jmdcme@asip.org