

JMD CME Program in Molecular Diagnostics 2008

American Society for Investigative Pathology *and the*
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CME Questions # 19-26

(See January and March Examination Sheets for Questions # 1-18)

19. More than 50 emerging and reemerging pathogens have been identified over the past four decades. Based on the referenced Review of the molecular diagnostics of emerging pathogens, select the ONE match between infectious agent and resulting disease that is NOT true: [See J Mol Diagn 2008 10:185-197; no authors of the referenced article disclosed any potential conflicts of interest.]

- a. *Bartonella henselae* causes cat scratch disease.
- b. Sin Nombre virus causes bacillary angiomatosis.
- c. *Anaplasma phagocytophilum* causes human granulocytotropic anaplasmosis.
- d. Nipah virus causes encephalitis.
- e. Marburg virus causes hemorrhagic fever.

20. Molecular assays have played critical roles in the discovery, surveillance, and clinical laboratory diagnosis of newly emerging and reemerging viral respiratory infections in recent years. Based on the referenced Review, select the ONE statement that is NOT true: [See J Mol Diagn 2008 10:185-197; no authors of the referenced article disclosed any potential conflicts of interest.]

- a. Influenza A has 10 H and 12 N subtypes, of which only subtypes H1, H2, and N2 have stable lineages in avian and human populations.
- b. H and N antigenic variants determined by point mutations cause seasonal influenza epidemics, whereas new antigenic H and N subtypes introduced by reassortment of viral genes cause pandemics.
- c. Influenza A has no pathognomonic symptoms, and diagnosis of influenza A based on clinical signs is correct in only two-thirds of patients.
- d. Several consensus and subtype-specific molecular assays have been developed to detect the four human coronaviruses (HCoV); however, the genetic variability of HCoVs makes the detection of all circulating strains technically challenging.
- e. Human bocavirus (HBoV) is a newly discovered human parvovirus with a worldwide distribution and a high prevalence of up to 18%.

21. Food-borne outbreaks of *Cyclospora cayatanensis* have occurred around the world. Based on the referenced Review, select the ONE statement that is NOT true: [See J Mol Diagn 2008 10:185-197; no authors of the referenced article disclosed any potential conflicts of interest.]

- a. *C. cayatanensis* was first described as a human pathogen in 1994.
- b. Infection occurs via the fecal-oral route by ingestion of contaminated water or produce.
- c. Human-to-human infection is very likely because of the short sporulation time after shedding in feces.
- d. *C. cayatanensis* oocytes are similar to those of *Cryptosporidium* but are twice the diameter.
- e. PCR detection of *C. cayatanensis* in human feces, produce, and water employs primers that target the internal transcribed spacer (ITS) region, with analytical sensitivity of 10 oocytes/gm of feces.

22. Molecular assays have played important roles in the identification, surveillance, and clinical diagnosis of emerging viral hepatitis. Based on the referenced Review, select the ONE statement that is NOT true: [See J Mol Diagn 2008 10:185-197; no authors of the referenced article disclosed any potential conflicts of interest.]

- a. Hepatitis E virus (HEV) is a non-enveloped single-stranded, positive-sense RNA virus that is transmitted enterically.
- b. No chronic sequelae develop after infection with HEV, but fulminant hepatitis occurs especially in pregnant women.
- c. The genomic organization of HEV is close to rubella virus.
- d. Hepatitis delta virus (HDV) requires hepatitis B virus (HBV) to complete its life cycle in the eukaryotic host cell.
- e. All patients co-infected with HBV and HDV develop cirrhosis and die of end-stage liver disease.

23. Acute myelogenous leukemia (AML) is a heterogeneous disease clinically, molecularly, and cytogenetically. Based on the referenced Commentary and related articles, select the ONE statement regarding new molecular diagnostic tests for cytogenetically normal AML that is NOT true: [See J Mol Diagn 2008 10:198-202; J Mol Diagn 2008 10:212-216; and J Mol Diagn 2008 10:236-241; no authors of the referenced articles disclosed any potential conflicts of interest.]

- a. Approximately 25% of adult AML and 10% of pediatric AML cases do not harbor genetic alterations that can be detected by conventional cytogenetics.
- b. In the 2001 World Health Organization (WHO) classification of AML, four recurrent cytogenetic abnormalities have been selected to define specific diagnostic entities, with favorable prognoses found in AMLs that harbor gene fusions resulting from t(8;21), t(15; 17) or inv(16).
- c. The prognosis of tumors with 11q23 translocations depends on the chromosomal partner.
- d. The use of targeted therapies such as all-*trans*-retinoic acid is essentially restricted to those AMLs with t(15;17) gene fusions.
- e. In approximately 5% of cases, bone marrow may be superior to peripheral blood in detecting clonal abnormalities.

24. Many recurrent genetic abnormalities have been identified in AML that are important in both tumorigenesis and clinical outcome. Based on the referenced Commentary and related articles, select the ONE statement that is NOT true: [See J Mol Diagn 2008 10:198-202; J Mol Diagn 2008 10:212-216; and J Mol Diagn 2008 10:236-241; no authors of the referenced articles disclosed any potential conflicts of interest.]

- a. Partial tandem duplications of *MLL* are associated with a poor prognosis.
- b. Internal tandem duplication within *FLT3* has a significantly adverse effect on clinical outcome.
- c. Translocations such as t(8;21) and t(15;17) that disrupt transcription factors (*RUNX1* and *RARA*, respectively) in a dominant-negative fashion lead to a block in normal myeloid differentiation (so-called class 2 mutations), but experimentally AML manifests only when translocations are combined with an additional mutation having a positive effect on proliferation (a so-called class 1 mutation).
- d. Mutations in *CEBPA* correlate with a poor prognosis.
- e. The most frequently identified mutated gene in cytogenetically normal AML is nucleophosmin (*NPM1*).

25. The *NPM1* gene is one of the most frequent targets of genetic alterations in hematopoietic tumors such as lymphomas and acute leukemia. Based on the referenced Commentary and related articles, select the ONE statement that is NOT true: [See J Mol Diagn 2008 10:198-202; J Mol Diagn 2008 10:212-216; and J Mol Diagn 2008 10:236-241; no authors of the referenced articles disclosed any potential conflicts of interest.]

- a. Point mutations in *NPM1* in AML all involve exon 6.
- b. Over 40 different types of mutations in the *NPM1* locus have been described so far, which result in the formation of different mutant proteins.
- c. Mutation A (*NPM1*-mutA) consists of a duplication of a TCTG tetranucleotide at position 956 to 959 of the reference sequence (GenBank accession number NM_002520).
- d. The clinical impact of *NPM1* mutations is affected by the mutational status of the *FLT3* gene.
- e. *NPM1* mutations are stable over the course of the disease and may serve as an ideal target for minimal residual disease assessment.

26. The analysis of *NPM1* mutational status is now recommended for inclusion in the routine genetic characterization of AML. Based on the referenced Commentary and related articles, select the ONE statement regarding new molecular diagnostic tests for cytogenetically normal AML that is NOT true: [See J Mol Diagn 2008 10:198-202; J Mol Diagn 2008 10:212-216; and J Mol Diagn 2008 10:236-241; no authors of the referenced articles disclosed any potential conflicts of interest.]

- a. A non-quantitative, genomic DNA-based PCR assay for detecting all known *NPM1* mutations has been developed that utilizes intronic primers to avoid the amplification of known pseudogenes.
- b. The relatively low analytic sensitivity of the genomic-DNA-based assay is not a limitation at initial diagnosis but it diminishes its utility for minimal residual disease detection.
- c. The genomic-DNA-based assay can be used on paraffin-embedded tissue.
- d. A methodology utilizing an RNA template that uses allele-specific oligonucleotide (ASO) primers detects over 40 *NPM1* mutations.
- e. The RNA ASO-based assay can detect mutant clones that represent as little as 0.001% of the population.

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

SEE EXAMINATION ANSWER SHEET – NEXT PAGE

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www.asip.org/CME/jmdCME.htm or www.amp.org/CME/jmdCME.htm**

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CME Questions # 19-26

Examination Answer Sheet #3, Questions #19-26					
Answer	a	b	c	d	e
Question #19	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Question #20	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Question #21	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Question #22	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Question #23	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Question #24	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Question #25	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Question #26	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Name					
Email Address					
CME ID# (For office use only)					

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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.

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