JMD CME Program in Molecular Diagnostics 2007

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

***The Journal of Molecular Diagnostics*, Volume 9, No. 5 (November 2007)**

http://jmd.amjpathol.org

www.asip.org/CME/jmdCME.htm

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CME Questions # 41-50
(See February-September Examination Sheets for Questions #1-40)

41. The clinical significance of micrometastasis of colorectal cancer to regional lymph nodes remains controversial. Based on the referenced Review article, select the ONE statement that is NOT true: [See J Mol Diagn 2007 9:563-571]

a. Colorectal cancer is the most common malignancy and third most common cause of cancer-related death in the United States.
b. The American Joint Committee on Cancer (AJCC) has defined micrometastases as lesions between 0.2 mm and 2.0 mm in diameter, and lesions smaller than 0.2 mm are referred to as "isolated tumor cells."
c. At a recent National Cancer Institute meeting, the term "occult tumor cells" was defined as disease that is not detected by standard techniques.
d. As opposed to breast cancer, there is a lack of information regarding occult, hematogenous metastasis in colorectal cancer.
e. Approximately 20 to 30% of patients with pathological-negative lymph nodes by current methods of analysis develop recurrent disease.

42. Improving the sensitivity and accuracy of occult tumor cell detection in colorectal cancer is an important goal. Based on the referenced Review article, select the ONE statement that is NOT true: [See J Mol Diagn 2007 9:563-571]

a. Current evidence suggests that a minimum of 8 lymph nodes be reviewed for accurate staging.
b. Attention to sample handling, such as warm ischemia time, is rarely addressed in the reviewed literature.
c. Studies were subject to sampling error depending on volume of the lymph node sampled.
d. A variety of antibodies have been used for immunohistochemical detection of occult disease in the lymph nodes of colorectal patients; however, a gold standard has not been clearly established.
e. CAM 5.2 is an antibody to cytokeratins CK8 and CK18, but it has been criticized as lacking specificity for colorectal cancer.

43. Several mRNA markers have been utilized for the detection of occult metastases in the lymph nodes of colorectal patients. Based on the referenced Review article, select the ONE statement that is NOT true: [See J Mol Diagn 2007 9:563-571]

a. All the reviewed studies that employed reverse transcription-polymerase chain reaction (RT-PCR) utilized CEA or CK20 mRNA markers.
b. One limitation of RT-PCR for the detection of occult disease is the potential for a lack of specificity due to low-level expression of the mRNA markers by lymphocytes or other cells present in benign lymph nodes.
c. A potential pitfall of epithelial cell-related markers is increased sensitivity at the expense of specificity.
d. Micrometastatic lymph node metastasis identified by RT-PCR was consistently found to be prognostically significant.
e. Micrometastatic lymph node metastasis identified by immunohistochemisty was consistently found to be prognostically significant.

44. Technological advances in DNA sequencing and array-based assays have expanded the diagnostic capabilities of molecular microbiology. Based on the referenced article and related Commentary, select the ONE statement that is NOT true: [See J Mol Diagn 2007 9:572-573 and J Mol Diagn 2007 9:624-630]

a. Ribosomal RNA (rRNA) gene sequencing is the current gold standard in microbial identification as well as the technical basis for modern bacterial taxonomy.
b. Molecular techniques are advantageous for clinical microbiology because they do not require culture, they have rapid turnaround times, and digital genetic information can be stored in databases for epidemiological studies.
c. Using an oligonucleotide microarray containing 16S rRNA, *katG*, and *rpoB* sequences, 27 of 27 mycobacterial species were correctly identified.
d. The Multi-Pathogen Identification microarray containing 53,660 oligonucleotide probes was developed to simultaneously detect 18 pathogens.
e. Using a microarray containing all 3,688 predicted coding DNA sequences from the sequenced strain *Clostridium difficil*e 630, it was shown that less than 20% of genes were shared by all strains, suggesting a high degree of genetic variability in this pathogen.

45. The use of pathogen genome sequence data for the control and management of infections remains an ongoing challenge. Based on the referenced article and related Commentary, select the ONE statement that is NOT true: [See J Mol Diagn 2007 9:572-573 and J Mol Diagn 2007 9:624-630]

a. Typhoid and paratyphoid fevers caused by *Salmonella enterica* serovars Typhi, Paratyphi A, Paratyphi B, and Paratyphi C pose significant health problems in many parts of the world.
b. Present-day vaccines are effective against *S.* Paratyphi only.
c. More than half of patients with culture-proven enteric fever in some geographic localities are infected with *S*. Paratyphi A.
d. Conventional diagnosis of enteric fever that relies upon isolation of the pathogen from blood, bone marrow aspirate and/or stool cultures and subsequent biochemical and serological testing of suspect isolates requires at least 4 to 8 days for final identification.
e. Increasing incidence of multi-antibiotic resistant Typhi and Paratyphi A strains and/or those exhibiting reduced susceptibility to fluoroquinolones threaten to undermine the efficacy of empirical therapy regimens.

46. The translation of genomics data into pathogen-specific PCR assays that yield predictive and diagnostic signatures for a wide range of pathogens is now possible. Based on the referenced article, select the ONE statement that is NOT true: [See J Mol Diagn 2007 9:624-630]

a. The MobilomeFINDER web server was used to perform *in silico* subtractive hybridization to identify 43 protein-coding sequences that were present in two Paratyphi A strains but not in other sequenced *Salmonella* genomes.
b. A multiplex PCR assay was developed that produced one of two distinct 4-band signatures, each of which was diagnostic of *S*. Parathyphi A.
c. A common *S*. Paratyphi A genetic polymorphism of the *stkF* gene was detected.
d. The MobilomeFINDER approach cannot be used to identify and map non-coding sequences.
e. The Paratyphi A-specific multiplex PCR assay permitted same-day identification of suspect bacterial isolates.

47. Hypermethylation of CG-rich promoter regions of tumor suppressor genes is a frequent event in carcinogenesis. Based on the referenced Technical Advance article, select the ONE statement that is NOT true: [See J Mol Diagn 2007 9:574-581]

a. Hypermethylation of repeated sequences in the genome has been shown to increase the homologous recombination and rearrangement of chromosomes.
b. Demethylation changes the expression of imprinted genes, tissue-specific genes, proto-oncogenes and genes associated with invasion and metastasis.
c. Non-bisulfite methodology to study the degree of DNA methylation relies on the digestion of DNA with methylation-sensitive restriction enzymes followed by PCR or Southern blot.
d. Bisulfite converts unmethylated cytosine to guanine.
e. Bisulfite conversion causes denaturation and degradation of DNA.

48. Detection of the methylation status of CpG islands of gene promoters can be a useful tool for the diagnosis of human diseases. Based on the referenced Technical Advance article, select the ONE statement that is NOT true: [See J Mol Diagn 2007 9:574-581]

a. A new PCR-based technique, named methyl-sensitive DMSO-PCR (Ms-DMSO-PCR), was developed for detecting the methylation status of gene promoters based on the finding that methylated and unmethylated DNAs show a different sensitivity to the amount of DMSO used in the amplification reaction.
b. The hypermethylation of *MGMT* has been shown to be useful predictor of the responsiveness of tumors to alkylating agents.
c. The *DAPK* promoter was hypomethylated in cancer samples compared to normal tissues.
d. The differential sensitivity to DMSO was linearly dependent on the C+G content of amplified fragments.
e. Primers designed for the Ms-DMSO-PCR test do not need to contain CG dinucleotides.

49. Classic galactosemia is an inherited autosomal recessive error of galactose metabolism. Based on the referenced article, select the ONE statement that is NOT true: [See J Mol Diagn 2007 9:618-623]

a. Over 200 mutations in the gene for galactose-1-phosphate uridyl transferase (GALT) have been identified in patients affected with galactosemia.
b. Deficiency of GALT results in a buildup of galactose-1-phosphate, leading to poor feeding, vomiting, diarrhea, and cataracts and, if left untreated, physical and mental retardation.
c. Two *GALT* mutations, p.Q188R and p.K285N, reportedly account for approximately 69 to 88% of galactosemia alleles in Caucasian populations.
d. The p.S135L is the most common mutation in African Americans and accounts for 50% of the mutations observed in that population.
e. The Duarte variant increases GALT enzyme activity by approximately 25% and is found exclusively in Hispanic populations.

50. *Chlamydia trachomatis* (Ct) is the most prevalent sexually transmitted bacterial pathogen. Based on the referenced article, select the ONE statement that is NOT true: [See J Mol Diagn 2007 9:631-638]

a. Although most Ct infections remain asymptomatic, when left untreated they can lead to pelvic inflammatory disease, ectopic pregnancy, and tubal infertility.
b. As a species, *C. trachomatis* can be divided into three serogroups and subsequently into 19 serovars.
c. Serovars B and C are commonly detected in the urogenital tract and the rectum.
d. The distribution of the serovars and serogroups showed a clear difference between samples from Uganda and The Netherlands.
e. Infection by serovars D, E, F, and G infection may be sustained for a longer period than the other serovars, which would result in more common detection of these serovars.

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

SEE EXAMINATION ANSWER SHEET – NEXT PAGE

TO REGISTER:
http://www.asip.org/CME/jmdCME07.htm or http://www.amp.org/CME/jmdCME2007.htm

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CME Questions # 41-50

Examination Answer Sheet #5, Questions #41-50					
Answer	**a**	**b**	**c**	**d**	**e**
Question #41	❍	❍	❍	❍	❍
Question #42	❍	❍	❍	❍	❍
Question #43	❍	❍	❍	❍	❍
Question #44	❍	❍	❍	❍	❍
Question #45	❍	❍	❍	❍	❍
Question #46	❍	❍	❍	❍	❍
Question #47	❍	❍	❍	❍	❍
Question #48	❍	❍	❍	❍	❍
Question #49	❍	❍	❍	❍	❍
Question #50	❍	❍	❍	❍	❍
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		CME ID# (For office use only)			

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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 AMP/ASIP JMD 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/register.html** or you may submit your CME 2007 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 AMP/ASIP JMD CME office at the completion of the 2007 CME year.

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