Continuing Education Questions

FALL 2007

To receive **2.0** contact hours of **intermediate** level. P.A.C.E.® credit for the **Focus: New Directions in Hemostasis and Coagulation** 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

Upon completion of this section, the reader will be able to:

1. compare and contrast the clinical symptoms and etiology of TTP and HUS.
2. name the enzyme responsible for cleaving ultra large von Willebrand factor molecules.
3. describe the clinical manifestations of a deficiency of this enzyme.
4. predict the most appropriate course of treatment for a patient with this enzyme deficiency.
5. correlate the clinical pathologic manifestations with the type of thrombosis (arterial vs venous).
6. compare and contrast the most important risk factors, the nature of the clot, and the target for therapeutic prevention and treatment for arterial and venous clot formation.
7. summarize the data suggesting a link between arterial and venous thrombosis.
8. identify the major components (cellular and inflammatory mediators) of inflammation.
9. describe the functions of the inflammatory response.
10. list the major inflammatory cytokines.
11. identify the significant effects of the inflammatory mediators on the coagulation and fibrinolytic systems.
12. identify the significant effects of the coagulation and fibrinolytic systems on inflammation.

CONTINUING EDUCATION QUESTIONS
THROMBOTIC MICROANGIOPATHY (TTP AND HUS): ADVANCES IN DIFFERENTIATION AND DIAGNOSIS

1. Both thrombocytopenic thrombotic purpura (TTP) and hemolytic uremic syndrome (HUS) present with microangiopathic hemolytic anemia. Which set of features best represents TTP?
   a. Verotoxin-producing E. coli, abdominal pain, diarrhea, decreased platelet count, and schistocytes on peripheral smear
   b. Abdominal pain, diarrhea, severely decreased platelet count, and schistocytes on peripheral smear
   c. Abdominal pain, diarrhea, severely decreased platelet count, and negative for schistocytes on peripheral smear
   d. Verotoxin-producing E. coli, abdominal pain, diarrhea, normal platelet count, and positive for schistocytes on peripheral smear

2. Ninety-five percent of these cases are found in children and are associated with infection by verotoxin-producing E. coli:
   a. HUS
   b. TTP
   c. MAHA
   d. TMA

3. The enzyme responsible for cleaving ultra-large von Willebrand factor molecules is:
   a. ULVWF enzyme.
   b. ADAMTS-23.
   c. ULVWF-13.
   d. ADAMTS-13.

4. A deficiency of the enzyme responsible for cleaving ultra-large von Willebrand factor molecules results in:
   a. thrombosis, bleeding and ULVWF molecules.
   b. UL endothelial cells, thrombosis and bleeding.
   c. small von Willebrand subunits and thrombosis.
   d. ULVWF molecules reacting with circulating platelets.

5. Clinically, a deficiency of the enzyme responsible for cleaving ultra-large von Willebrand factor molecules results in:
   a. formation of microthrombi leading to cerebral infarction and renal failure.
   b. a tendency to joint bleeding.
   c. ecchymosis and petechiae.
   d. lack of clinical symptoms making diagnosis difficult.

6. A patient suffering from a deficiency of the enzyme responsible for cleaving ultra-large von Willebrand factor molecules would best be treated by:
   a. a single treatment with plasmapheresis.
   b. removal of the spleen and a single treatment with plasmapheresis.
   c. daily plasmapheresis until the platelet count returns to normal.
   d. infusion of fresh frozen plasma without plasmapheresis.

IS THERE A GENETIC RELATIONSHIP BETWEEN ARTERIAL AND VENOUS THROMBOSIS?

7. Venous thrombosis is generally associated with:
   a. acute myocardial infarction.
   b. pulmonary embolism.
   c. non-hemorrhagic cerebrovascular accidents.
   d. atherosclerotic vascular disease.

8. Arterial thrombosis is traditionally characterized by all of the following EXCEPT:
   a. formation of white clots, rich in platelets.
   b. atherosclerotic vascular injury.
   c. changes in blood composition (thrombophilia).
   d. treatment generally with anti-platelet agents.

9. Which of the following supports the concept that arterial thrombosis and venous thrombosis are linked pathophysiologic processes?
   a. Individuals experiencing a secondary venous thromboembolic events (VTE) have a greater risk of carotid artery plaque formation and atherosclerosis than those experiencing an idiopathic VTE.
   b. Individuals experiencing an idiopathic venous thromboembolic event are more likely to suffer a significant arterial event than the general population.
   c. Individuals experiencing an idiopathic VTE and individuals experiencing a secondary VTE have the same likelihood of having metabolic syndrome.
   d. The Genetic Susceptibility to Thrombosis (GAIT) study showed a stronger correlation with venous thrombosis than arterial trombosis.

CROSS TALK BETWEEN THE INFLAMMATION AND COAGULATION SYSTEMS

10. Which of the following cells is NOT considered a significant contributor to inflammation?
    a. Lymphocytes
    b. PMNs (neutrophils)
    c. Basophils/mast cells
    d. Platelets

11. Which of the following best describes the function of the inflammatory response?
    a. To activate natural killer (NK) cells as part of the host defense
    b. To neutralize or eliminate pathogens (or to destroy injured or necrotic tissue) as part of the host defense
    c. To activate cytotoxic T lymphocytes as part of the host defense
    d. To stimulate antibody production by B lymphocytes

12. All of the following are considered important inflammatory cytokines EXCEPT:
    a. Tumor Necrosis Factor (TNF).
    b. Interleukin-6 (IL-6).
    c. Interleukin-1 (IL-1).
    d. Interleukin-3 (IL-3).

13. The effect of inflammation on the protein C anticoagulant system is to:
    a. decrease thrombomodulin.
    b. decrease C4b binding protein (C4bBP).
    c. increase endothelial cell protein C receptor (ECPR).
    d. increase protein C and protein S.

14. Which of the following statements concerning the effect of inflammation on the hemostatic system is correct?
    a. Induces thrombocytopenia and dysfunctional platelets activation
    b. Increases activity of coagulation inhibitors such as antithrombin (AT) and tissue factor pathway inhibitor (TFPI)
    c. Increases procoagulant activity of the endothelium
    d. Increases activity of the fibrinolytic system

15. Thrombin and other coagulation proteases activate cells via binding to PAR receptors. PAR stands for:
    a. prothrombin associated receptor.
    b. pathogen activated receptor.
    c. plasminogen associated receptor.
    d. protease activated receptor.

16. The major effect of the procoagulant inhibitors, antithrombin (AT), activated protein C (APC), and tissue factor pathway inhibitor (TFPI) on inflammation is to:
    a. decrease the production of inflammatory mediators and leukocyte activation.
    b. inhibit the vascular changes seen during the inflammatory response.
    c. stimulate endothelial cells to upregulate thrombomodulin (TM) and endothelial cell protein C receptor (EPCR).
    d. promote leukocyte adhesion and migration.

17. The role of thrombin activated fibrinolysis inhibitor (TAFI) in inflammation is to:
    a. activate proinflammatory mediators such as bradykinin.
    b. inactivate C3a and C5a.
    c. inhibit leukocyte adhesion to the endothelium.
    d. induce leukocyte chemotaxis into the tissues.

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Answers
Circle correct answer.

1.	a	b	c	d	10.	a	b	c	d
2.	a	b	c	d	11.	a	b	c	d
3.	a	b	c	d	12.	a	b	c	d
4.	a	b	c	d	13.	a	b	c	d
5.	a	b	c	d	14.	a	b	c	d
6.	a	b	c	d	15.	a	b	c	d
7.	a	b	c	d	16.	a	b	c	d
8.	a	b	c	d	17.	a	b	c	d
9.	a	b	c	d					

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Please circle the most appropriate answers.

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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?

Continuing Education Questions

FALL 2007

To receive **2.0** contact hours of **intermediate** level P.A.C.E.® credit for the **Focus: Proteomics** 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

Upon completion of this section, the reader will be able to:

1. compare and contrast gene expression versus protein expression.
2. discuss the purpose and goals of proteomics.
3. identify the steps followed in a proteomic analysis.
4. describe the main techniques used in proteomics.
5. recognize the different tools applied to proteomics analysis.
6. differentiate the procedures utilized in proteomics studies starting from protein sample preparation to protein identification methods.
7. identify the steps needed for analysis of protein expression by software packages.
8. distinguish the methods employed for qualitative and quantitative protein identification.
9. present an overview of proteomics methodology.
10. comprehend how proteomic methodology is applied in the medical field.
11. describe the potential application of clinical proteomics in the development of new biomarkers in diagnostic and prognostic tests.

CONTINUING EDUCATION QUESTIONS
INTRODUCTION TO PROTEOMICS

1. The scientific approach to analyze all proteins expressed by a genome is known as:
   a. the Human Genome Project.
   b. proteome.
   c. proteomics.
   d. gene analysis.

2. The main goal of proteomics is to:
   a. identify and characterize altered protein expression.
   b. investigate co-and posttranslational protein modification.
   c. correlate protein structure and function with biological activity.
   d. all of the above.

3. Objectives of clinical proteomics are all of the following EXCEPT:
   a. identify proteins involved in pathological processes.
   b. identify processes of protein expression.
   c. understand how changes in protein expression cause illness.
   d. develop biomarkers for diagnosis and therapeutic interventions.

4. In certain genes, the combination of exons can make a gene become active and each combination may result in a different protein. This process is known as:
   a. alternative splicing.
   b. RNA splicing.
   c. RNA processing.
   d. gene processing.

5. Eukaryotic gene expression and regulation at the transcriptional level occur by all of the following EXCEPT:
   a. RNA splicing.
   b. RNA processing.
   c. polyadenylation.
   d. chemical alteration.

6. Post-transcriptional modifications of proteins occur by all of the following EXCEPT:
   a. acetylation.
   b. glycosylation.
   c. polyadenylation.
   d. phosphorylation.

7. Expression proteomics differs from functional proteomics in that:
   a. expression proteomics analyzes and evaluates protein activity.
   b. expression proteomics analyzes protein-protein interactions.
   c. expression proteomics compares the expression profiles of protein patterns.
   d. expression proteomics understands signaling mechanisms involving pathological conditions.

8. Which of the following techniques has been considered for the past 20 years the standard technique for analyzing proteins?
   a. UV spectroscopy
   b. Two-dimensional electrophoresis
   c. Stepwise chemical degradation
   d. None of the above

9. The chronological order for identification of proteins using 2-DE is:
   a. protein separation by mass spectrometry followed by separation by isoelectric point followed by molecular weight.
   b. protein separation by molecular weight followed by separation by isoelectric point followed by mass spectrometry.
   c. protein separation by mass spectrometry followed by separation by molecular weight followed by isoelectric point.
   d. protein separation by isoelectric point followed by separation by molecular weight followed by mass spectrometry.

10. The mass spectrometry techniques used for the identification of proteins are all the following EXCEPT:
    a. Matrix-Assisted Laser Desorption Ionization – time-of-flight (MALDI-TOF).
    b. Liquid Crystal Multiple Sequence Mass Spectrometry (LC-MS-MS).
    c. Electrospray Ionization tandem Mass Spectrometry (ES-MS/MS).
    d. Surface Enhanced Laser Description Ionization (SELDI).

PROTEOMICS TECHNOLOGY

11. The most important factor during protein sample preparation is:
    a. nucleic acid digestion.
    b. protein solubilization.
    c. protein aggregation.
    d. enzymatic degradation.

12. The main goal of protein sample preparation is to:
    a. increase protein aggregation and use reducing agents such as chaotrops and detergents to improve solubility.
    b. avoid protein sample pre-fractionation and increase the solubility of the sample.
    c. increase protein solubility, reduce complexity, and eliminate nucleic acid.
    d. increase solubility and complexity while enhancing enzymatic and chemical degradation.

13. Methods used to reduce protein complexity are all of the following EXCEPT:
    a. subcellular fractionation.
    b. selective fractionation.
    c. chromatography.
    d. pre-fractionation.

14. The mass spectrometry techniques used for the identification of proteins include all of the following EXCEPT:
    a. Matrix-Assisted Laser Desorption Ionization – time-of-flight (MALDI-TOF).
    b. Electromagnetic Ionization – MS/MS (EM-MS).
    c. Isotope-coded Affinity Tagging (ICAT).
    d. Surface Enhanced Laser Description Ionization (SELDI).

15. All of the following are true concerning first dimension 2-DE EXCEPT:
    a. cup loading of the sample should be used to decrease production of artifacts.
    b. the isoelectric point of the protein is determined using immobilized pH gradients.
    c. a broad-range pH gradient is used to obtain a reference map of the majority of proteins.
    d. nonlinear pH gradients improve visualization of proteins in the middle of pH range.

16. The five chronological steps in a classical 2-DE analysis are:
    a. protein spot detection, matchset generation, normalization, protein spot quantitation, and statistical analysis.
    b. normalization, protein spot detection, matchset generation, quantitation of protein spots, and statistical analysis.
    c. matchset generation, protein spot detection, protein spot quantitation, normalization, and statistical analysis.
    d. protein spot detection, normalization, protein spot quantitation, matchset generation, and statistical analysis.

17. The chronological order of the three basic steps involved in mass spectrometry is:
    a. analyzer detection, ionization of protein molecules, and mass-to-charge ratio separation.

b. mass-to-charge ratio separation, analyzer detection, and ionization of protein molecules.
c. ionization of protein molecules, analyzer detection, and mass-to-charge ratio separation.
d. ionization of protein molecules, mass-to-charge ratio separation, and analyzer detection.

18. What is the major difference in protein analysis between MALDI and ESI?
    a. MALDI protein analysis occurs in solid phase and ESI analysis occurs in liquid phase.
    b. Maldi analysis uses a liquid phase and ESI analysis occurs in a gas phase.
    c. Maldi analysis is performed in a liquid phase and ESI occurs in a solid phase.
    d. Maldi analysis is performed in a gas phase and ESI occurs in a liquid phase.

19. All of the following are true concerning ICAT EXCEPT:
    a. that it omits the 2-DE separation.
    b. that it requires free cysteine residues on the protein being labeled.
    c. that it is unable to quantitate proteins from a complex mixture.
    d. that it is possible to compare the proteins present in two proteomes.

20. In second dimension 2-DE all proteins previously separated via first dimension 2-DE are subsequently separated according to their molecular weight. This is accomplished by using:
    a. uniform concentration of acrylamide gels for broad pH range.
    b. different concentrations of acrylamide gels.
    c. short run times for large gels.
    d. long run times for mini-gels.

PROTEOMICS: CLINICAL APPLICATIONS

21. Clinical proteomics offers the opportunity to:
    a. develop new diagnostic tests.
    b. develop new prognostic tests.
    c. identify new therapeutic targets.
    d. all of the above.

22. Which of the following is the most common technique used in proteomics technology?
    a. Immunochemical electrophoresis
    b. Bioinformatics
    c. Mass spectrophotometry
    d. Two-dimensional electrophoresis

23. All of the following are challenges to proteomic clinical application except:
    a. optimization of low abundance protein detection.
    b. analysis of bacterial virulent strains of protein expression.
    c. software development for data acquisition.
    d. correlation, validation, and interpretation of clinical data.

24. Proteomic technology includes which of the following?
    a. Separation of protein by their molecular weight and isoelectric point
    b. Removal and identification of specific proteins
    c. Enzymatic digestion and ionization of protein particles
    d. a, b, and c

25 Many tumor markers lack specificity and sensitivity. In contrast, the use of proteomics applications in diagnosis and prognosis of cancer offers a more reliable biomarker by detecting:
    a. albumins and globulins.
    b. aberrant proteins.
    c. carrier proteins.
    d. proteins with high mass/charge ratio.

26. Alpha-beta cystallin and tropomyosin are examples of clinical proteomic application correlates with:
    a. cardiac allograft rejection.
    b. ovarian cancer.
    c. lung cancer.
    d. cardiomyopathy.

27. Proteomics methodology in microbiology can be simplified by the use of:
    a. bacterial organelles.
    b. bacterial cloning.
    c. bacterial protein enriched fractions.
    d. whole bacteria protein.

28. Important issues in the clinical application include all of the following except:
    a. specimen collection and processing.
    b. standardization of protein output.
    c. patient's biorhythm.
    d. accurate calibration of instruments.

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6.	a	b	c	d	20.	a	b	c	d
7.	a	b	c	d	21.	a	b	c	d
8.	a	b	c	d	22.	a	b	c	d
9.	a	b	c	d	23.	a	b	c	d
10.	a	b	c	d	24.	a	b	c	d
11.	a	b	c	d	25.	a	b	c	d
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