PULMONARY AND VTE QUESTIONS

ACS CRITICAL CARE REVIEW COURSE

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1. Which of the following is TRUE regarding antibiotic treatment of ventilator-associated pneumonia (VAP)?

   A. Initiating antibiotic therapy early before culture results return promotes growth of resistant organisms

   B. Initial empiric antibiotic choice should be individualized based on each patient's disease process

   C. Short courses of treatment (7 or 8 days) consistently result in higher recurrence rates than longer courses of treatment ($\geq$ 14 days)

   D. Pseudomonas VAP may be treated with single-drug coverage as long as the culture sensitivities and MIC (minimum inhibitory concentration) are adequate

The scientific basis for antibiotic therapy of VAP has been significantly advanced in the last 5 to 10 years. It is now clear that even a short delay in administration of antibiotics for patients being investigated for VAP results in a higher mortality rate. Broad spectrum antibiotics, to include coverage of MRSA, must be administered as soon as the diagnosis is suspected either by clinical criteria or by preliminary Gram stain of a sputum sample. This early, broad, empiric coverage is coupled with the so-called "de-escalation" to more targeted antibiotics (usually a single agent) based on the results of cultures and their sensitivities and MIC values. Initial use of these broad empiric antibiotics has not been shown to promote antibiotic resistance, but has been shown to reduce mortality. The choice of agents is based on coverage of all common Gram positive and Gram negative pathogens associated with VAP, ideally tailored to a hospital's local antibiograms, but should not be individualized for different (immunocompetent) patients. Duration of treatment has long been subjective and non evidence-based. Several recent randomized trials have demonstrated the efficacy of short courses of therapy compared to traditional courses of 14 days or longer, with similar outcomes and recurrence rates. While longer courses are associated with similar overall recurrence rates, they result in a higher recurrence with multi-drug resistant organisms. However, an exception to using short course therapy must be made when the causative pathogen is a non-fermenting Gram

negative bacillus (Pseudomonas, Acinetobacter, Stenotrophomonas), which do have higher recurrence rates when treated with shorter courses. The long-standing dogma of "double-coverage" of Pseudomonas species has not been borne out consistently. Treatment with a single antibiotic is sufficient, assuming, as with any causative organism, that the pathogen is sensitive and an antibiotic with a low MIC is chosen.

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Chastre J, Wolff M, Fagon JY, et al. Comparison of 8 vs 15 days of antibiotic therapy for ventilator-associated pneumonia in adults: a randomized trial. JAMA. 2003;290(19):2588-2598.

2. Which statement regarding ventilator-associated pneumonia (VAP) is TRUE?

    A. Diagnosis of VAP based on clinical criteria results in less antibiotic use when compared to diagnosis using quantitative cultures

    B. Evidence-based use of stress ulcer prophylaxis and venous thromboembolism prophylaxis reduces the incidence of VAP

    C. VAP rates as reported by the CDC have been declining over the past decade in both medical and surgical intensive care units

    D. After intubation occurs, the risk of acquiring VAP cannot be directly modified

Diagnosis of VAP is a controversial and evolving topic. There is no widely accepted, standardized method of diagnosis that has both high sensitivity and specificity. The clinical diagnostic strategy requires a lung infiltrate along with 2 or more of the following: leukocytosis or leukopenia, fever or hypothermia, purulent sputum, and decreasing oxygenation. Since this method is nonspecific (many critically ill patients with fever, leukocytosis, and infiltrates do not have pneumonia), it results in overtreatment

(treating patients with antibiotics who do not have VAP) and more antibiotic use than a strategy employing quantitative cultures to confirm the diagnosis. VAP prevention programs are essential to reduce the incidence of this hospital acquired infection, and such programs include techniques that either directly or indirectly reduce the risk of VAP. Direct methods include avoiding intubation in the first place, elevation of the head of the bed, and continuous suctioning of subglottic secretions. Indirect methods include practices that reduce the time spent on the ventilator, such as ventilator protocols, daily assessment for extubation, and interruption of continuous sedation drips. While stress ulcer and VTE prophylaxis are part of the "ventilator bundle", and prevent complications associated with being critically ill and on mechanical ventilation, they have no direct effect on the risk of developing VAP. However, use of known VAP prevention techniques does reduce the risk of VAP after intubation. The CDC's National Healthcare Safety Network (NHSN) has reported VAP rates from a sample of intensive care units across the U.S. since 2004 (and prior to that via the National Nosocomial Infection Surveillance System or NNIS). VAP rates in these reports have been steadily declining in all types of patient populations. According to the CDC, Medical ICUs have lower VAP rates than Surgical ICUs, while Trauma ICUs have the highest rates. Whether this decline in VAP rates is due to employment of prevention strategies or reflects hospitals' use of different methods of reporting rates to the CDC is unknown.

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Edwards JR, Peterson KD, Banerjee S, et al. National Healthcare Safety Network (NHSN) Report, Data summary for 2006 through 2008, issued December 2009. Am J Infect Control 2009:37:783-805.

Isakow W, Kollef MH. Preventing ventilator-associated pneumonia: an evidence-based approach of modifiable risk factors. Semin Respir Crit Care Med. 2006;27(1):5-17.

3. A patient with acute respiratory distress syndrome and a PaO2/FIO2 ratio of 150 is turned from the supine position to the prone position, with no change in ventilator settings. The PaO2/FIO2 ratio an hour later is 185. The improved oxygenation is due to all of the following except:

   A. decreased anatomic shunt

   B. decreased alveolar-arterial gradient

   C. decreased V/Q mismatch in zone 3 of the lungs

D. decreased transpulmonary shunt

In ARDS, the dependent portions of the lungs experience consolidation and alveolar collapse secondary to noncardiogenic edema, inflammation, decreased clearance of secretions, and compression from the weight of the more anterior lung tissue. This results in well perfused but poorly ventilated posterior lung fields (zone 3). As a result, gas exchange between zone 3 alveoli and blood from the pulmonary arteries is poor, and this oxygen-poor blood is mixed with oxygenated blood from better ventilated lung segments, lowering the overall PaO2 in the systemic circulation. The term shunt describes the flow of suboptimally oxygenated blood to the left side of the heart. The intra- or transpulmonary shunt refers to blood that passes through the capillaries of poorly ventilated or nonventilated alveoli, while the anatomic shunt refers to blood that perfuses the bronchial tree itself and vessels that empty directly into the left heart without passing through the pulmonary arterial circulation (thebesian veins). The anatomic shunt is fairly constant, and cannot be clinically manipulated to improve oxygen content. The transpulmonary shunt, if not a complete shunt (that is, there is some degree of ventilation) can be improved by inspiration of 100% oxygen, or by improving the matching of ventilation and perfusion in the lung itself. In ARDS patients, when the poorly ventilated posterior lung segments are put in the anterior position by proning, these areas are then better ventilated and oxygen exchange is improved. Likewise, the previously anterior segments that were not consolidated are exposed to improved blood flow when changed to a posterior position. Both anterior and posterior segments experience a decrease in their degree of ventilation/perfusion mismatch, and with improved oxygen exchange, the difference between the pO2 in the alveoli and the capillaries decreases (i.e. the pO2 of blood leaving the capillaries increases). With time however, the newly dependent lung fields may become consolidated themselves, worsening the shunt.

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Bartlett RH. Respiratory Physiology and Pathophysiology. In *Critical Care Physiology*. Bartlett RH, ed. Little, Brown, and Company, Inc. 1996;48-100.

4. Which of the following anticoagulants is not indicated in the treatment of venous thromboembolism (VTE) once a diagnosis of heparin-induced thrombocytopenia is established:

A. Lepirudin

B. Argatroban

C. Fondaparinux

D. Dalteparin

Heparin-induced thrombocytopenia (HIT) and heparin-induced thrombocytopenia with thrombosis (HITTS) may develop in 1-5% of patients exposed to heparin products, typically between 3 and 14 days after exposure, although may be sooner in patients with previous exposure. Heparin-induced thrombocytopenia should be suspected when there is a 50% or more decrease in the platelet count, the platelet count drops below 100,000 cells/microL, or thrombosis is noted during anticoagulation. Nonimmune- (HIT) and immune-mediated (HITTS) processes are described, the latter in which heparin-dependent antibody binds to platelet factor 4 forming a heparin-PF4-antibody complex. This complex activates platelets causing aggregation and removal from circulation, leading to thrombocytopenia with or without thrombosis. Lepirudin and argatroban are direct thrombin inhibitors and do not bind to platelet factor 4. Both lepirudin and argatroban are indicated in the treatment of HIT/HITTS. Fondaparinux is a factor Xa inhibitor and also does not bind to platelet factor 4. Recent evidence suggests fondaparinux may be used to treat HIT/HITTS as well. Dalteparin is a low-molecular-weight heparin similar to enoxaparin, and while the incidence of HIT is decreased compared to unfractionated heparin, it is not zero. Therefore, dalteparin is the correct answer.

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Villalba MR, Schreiber MA. Coagulopathies, thrombotic disorders, and blood component therapy. In: Roberts PR, Todd SR, eds. *Comprehensive Critical Care: Adult.* Mount Prospect, IL: Society of Critical Care Medicine;2012:551-570.

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5. All of the following result in improved outcomes in surgical embolectomy for massive pulmonary embolism with hypotension, *except* when the operation is:

   A. Performed prior to cardiac arrest

   B. Performed using cardiopulmonary bypass

   C. Performed with routine placement of an inferior vena caval filter

   D. Performed on patients with out-of-hospital arrest in whom spontaneous circulation has been restored

Surgical embolectomy has been traditionally reserved for patients with massive, central pulmonary embolism and hypotension in which thrombolytics are either not successful or are contraindicated (recent surgery, active internal bleeding, history of intracranial hemorrhage, intracranial/spinal surgery within 3 months, intracranial tumor/AVM/aneurysm, bleeding diasthesis, severe uncontrolled hypertension, or stroke within 2 months), or in patients who fail percutaneous embolectomy. Morbidity and mortality have been historically as high as 30%, although improved outcomes including an operative mortality of 6% and an 83-92% three year survival have been recently quoted in the literature. Death and complications are lowest when surgical embolectomy is performed prior to cardiogenic shock or cardiac arrest; when performed on a warm, beating heart without aortic cross-clamping, cardioplegia, or fibrillation; when routinely placing an inferior vena caval filter; when operating on patients with out-of-hospital arrest in whom spontaneous circulation has been restored; and when not operating on the elderly. Computed tomography has been used to localize the embolus preoperatively, although echocardiography that documents right ventricular dysfunction/strain (surrogate for pulmonary embolism in TTE) in an unstable patient may be all that is required prior to operation.

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