CRITICAL CARE ALERT®

A monthly update of developments in critical care and intensive care medicine

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INSIDE

Financial Disclosure: *Critical Care Alert*'s editor, David J. Pierson, MD, nurse planner Leslie A. Hoffman, PhD, RN, and peer reviewer William Thompson, MD, report no financial relationships related to this field of study.

Can BNP Levels Be Used To Distinguish ARDS from Cardiogenic Pulmonary Edema?

ABSTRACT & COMMENTARY

By Andrew M. Luks, MD

Pulmonary and Critical Care Medicine, University of Washington, Seattle

Dr. Luks reports no financial relationship to this field of study.

Synopsis: *When used in conjunction with clinical and radiographic data, brain natriuretic peptide levels may provide a non-invasive alternative for distinguishing between ARDS and cardiogenic pulmonary edema in patients with severe hypoxemic respiratory failure.*

Source: Karmpaliotis D, et al, *Chest.* 2007;131(4):964-971.

BRAIN NATRIURETIC PEPTIDE (BNP) LEVELS HAVE BEEN SHOWN to be useful in distinguishing between cardiac and non-cardiac causes of dyspnea in patients who present to the emergency department with an unclear clinical picture. Karmpaliotis and colleagues sought to determine whether this non-invasive test could also be used to distinguish between the acute respiratory distress syndrome (ARDS) and cardiogenic pulmonary edema (CPE) in ICU patients with severe hypoxemic respiratory failure. The authors enrolled medical or surgical ICU patients with a P_aO_2/F_IO_2 ratio < 300 mm Hg, with bilateral pulmonary infiltrates on chest radiograph, and diagnostic uncertainty requiring insertion of a pulmonary artery catheter to facilitate diagnosis. They excluded patients with acute or chronic renal failure, recent coronary artery bypass grafting, prior measurement of BNP during that admission, and known left heart failure with ejection fraction < 30%.

A single investigator performed all pulmonary capillary wedge pressure (PCWP) measurements, and BNP levels were measured using the Triage Biosite immunoassay. Ten days after study enrollment, two intensivists, who were blinded to the results of the BNP testing, reviewed all the diagnostic information and, using the

American-European consensus conference definition of ARDS, categorized patients as having ARDS, CPE or a mixed picture (this last category was not defined by the authors). They created receiver operating characteristic (ROC) curves and determined the sensitivity, specificity and positive- and negative predictive values of BNP for the diagnoses of ARDS and CPE. Multivariable logistic regression was used to assess for an association between BNP and the final diagnosis and to evaluate for a relationship between BNP and in-hospital mortality.

Eighty patients completed the study. While mean BNP levels were significantly lower in ARDS than in CPE (325 pg/ml vs 1,260 pg/ml), BNP had a poor correlation (r = 0.27) with PCWP. The area under the ROC curve for BNP in the diagnosis of ARDS was 0.80. Using a cut-point of < 200 pg/ml, BNP had a specificity of 91% and a positive predictive value of 91% for the diagnosis of ARDS, while a cut-point of > 1200 pg/ml had a specificity of 92% and a positive predictive value of 75% for the diagnosis of CPE. In multivariate analysis, higher concentrations of BNP were associated with a lower likelihood of the diagnosis of ARDS. Among the separate categories of ARDS and CPE patients, higher BNP levels were associated in multivariate analysis with increased mortality.

Critical Care Alert, ISSN 1067-9502, is published monthly by AHC Media LLC, 3525 Piedmont Road., NE, Building. 6, Suite 400, Atlanta, GA 30305.

SENIOR VICE PRESIDENT/GROUP PUBLISHER: Brenda Mooney.

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MARKETING MANAGER: Shawn DeMario.

GST Registration Number: R128870672.

Periodicals postage paid at Atlanta, GA.

POSTMASTER: Send address changes to ***Critical Care Alert,*** P.O. Box 740059, Atlanta, GA 30374.

Back issues: $40.

Missing issues will be fulfilled by customer service free of charge when contacted within one month of the missing issues date.

This is an educational publication designed to present scientific information and opinion to health professionals, to stimulate thought, and further investigation. It does not provide advice regarding medical diagnosis or treatment for any individual case. It is not intended for use by the layman.

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COMMENTARY

In the wake of many studies showing either no benefit or possible harm from the use of Swan-Ganz catheters, this study provides a potentially useful addition to the diagnostic armamentarium in the ICU. Given the mortality benefit associated with low-tidal volume ventilation in ARDS, making the correct diagnosis is of great importance and the BNP assay may provide a rapid, non-invasive means by which this objective can be achieved.

In considering the usefulness of the test, however, several points warrant emphasis. First, this trial examined only 80 patients and, as the authors themselves state, further studies are necessary to validate these findings before instituting large changes in current practice. It is also important to note that the 200 pg/ml cut-point used for the diagnosis of ARDS in this study is higher than the cut points (80 pg/ml) used in the original emergency department studies that established the utility of the BNP assay in distinguishing between pulmonary and cardiac causes of dyspnea. Mistaken application of this lower threshold in the ICU could lead to inappropriate exclusion of ARDS and failure to institute low-tidal-volume ventilation in situations where it is actually warranted. Finally, the results of this trial make it clear that BNP levels correlate poorly with the PCWP and cannot be used as a surrogate marker for that variable. If accurate information about filling pressures is needed, invasive measurements may still be necessary.

Invasive Aspergillosis in the ICU

ABSTRACT & COMMENTARY

By David J. Pierson, MD, Editor

Synopsis: *With better immunosuppressive therapy and ICU care, invasive aspergillosis is being encountered more often. Making the diagnosis is challenging, especially in lower-risk patients such as those with COPD and cirrhosis. Despite availability of effective new antifungal agents with less toxicity than amphotericin B, the effectiveness of these drugs in critically ill patients is uncertain, and the prognosis remains poor.*

Source: Meersseman W, et al. *Clin Infect Dis.* 2007;45:205-216.

Meersseman and colleagues at Gasthuisberg University Hospital in Leuven,

Belgium, have extensive experience in studies of invasive aspergillosis (IA) in critically ill patients, including those without the traditional risk factors.[1] In this comprehensive review, these investigators summarize current knowledge of the risk factors, clinical manifestations, available diagnostic techniques, and treatment of IA, focusing on patients in the ICU.

In the general inpatient hospital population, invasive fungal infections have become more prevalent during the last 10-15 years. Much of this increase is accounted for by IA, although few data on IA specifically in critically ill patients have been published. Patients with neutropenia (less than 500 neutrophils/mL) are at the highest risk for IA, as are those with hematologic malignancies and allogenic bone marrow transplants. However, categories of patients who are at lower but still-substantial risk have increasingly been identified. These include those with prolonged treatment with corticosteroids prior to ICU admission, and patients with solid-organ cancer, HIV infection, lung and autologous bone marrow transplantation, and systemic diseases requiring immunosuppressive therapy. Also recognized as being at increased risk for IA are patients with COPD and cirrhosis, particularly in the latter case if they have been in the ICU for more than 1 week. Patients at relatively lower risk for IA include those with burns, other solid-organ transplants (ie, kidney, heart, or liver), prolonged ICU stays, malnutrition, and treatment with corticosteroids for 1 week or less.

Because of increased awareness of the possibility of invasive fungal infections in ICU patients who are being evaluated for prolonged fever or pulmonary infiltrates, it has become commonplace to send sputum, blood, and other microbiology specimens for fungal culture as well as for routine bacteriology. In an attempt to improve the efficiency of the microbiology services in their hospital, Bouza and colleagues in Madrid evaluated 404 isolates of *Aspergillus fumigatus* in 260 patients, 37% of whom were in ICUs or special hematology wards.[2] In their study, *A. fumigatus* was isolated 2.1 times per 1,000 admissions, and 1 time per 1,000 microbiology samples, representing 5.6% of the total fungal isolations during the 3-year study period. These investigators used clinical information about the patients with positive cultures to derive a predictive model for the probability of their having IA (*see Table 1*).

Table 1:

Performance of Predictive Model for Probability of Invasive Aspergillosis (IA) using Data from 260 Patients [data from Bouza et al[2]]

Score*	Patients with IA
0	2.5% (3/119)
1-2	10.3% (11/106)
3-4	40% (10/25)
5 or more	70% (7/10)

*Scoring scheme:		
	1 point:	2 or more positive airway samples
	1 point:	positive sample from an invasive procedure
	2 points:	leukemia
	2 points:	corticosteroid therapy
	5 points:	neutropenia

In their study of 102 patients with positive cultures for aspergillus in their medical ICU,[1] Meersseman et al found that almost all of them had required mechanical ventilation. Of the 56 patients with IA (26 with underlying hematological malignancy and 30 without malignancy), more than half had evidence of IA at the time of ICU admission. Individual case reports suggest that some patients acquire the infection while in the ICU, although available evidence indicates that most cases involve activation or progression of previously acquired infection in the context of critical illness.

Clinical presentations of IA most often encountered in the ICU include (a) the aggressive, angio-invasive form typically seen in neutropenic patients, (b) cavitating pulmonary infiltrates most often observed in patients on corticosteroids, those with COPD or cirrhosis, or in solid-organ transplant recipients, (c) anastomotic infections in lung transplant recipients, and, rarely, (d) miscellaneous presentations such as wound infections, mediastinitis (in cardiac surgery patients), and endocarditis.

The diagnosis of IA in ICU patients who are not in the classic high-risk category is challenging, because the presentation tends to be clinically nonspecific and the sensitivity and specificity of most commonly used tests vary. Angio-invasive IA typically produces multiple small nodules with characteristic halos on chest CT, but these signs are seldom present in patients in the lower-risk categories. Most patients in these categories are in the ICU because of processes—such as pneumonia or acute lung injury—whose clinical and radiographic signs obscure or mimic those of IA.

Cultures of respiratory specimens in such patients are both insensitive and nonspecific, and fungal stains of such specimens are negative in at least half of patients subsequently proven to have IA. Serologic tests such as galactomannan and β-$^{1,3}_{D}$-glucan, and PCR techniques for detection of fungal DNA, are increasingly available, although very few published data on the effectiveness of these tests are from ICU patients. In one study of IA in a general medical ICU population, serum galactomannan was positive in only 53% of patients with documented IA.[1] Although there has been the suggestion that this test is more sensitive in bronchoalveolar lavage fluid (BALF) than in serum, this is yet to be confirmed, and making the diagnosis continues to be challenging.

For ICU patients in all risk categories, IA carries a very unfavorable prognosis and responds poorly to available antifungal therapies. Voriconazole has recently become the standard of care for treating IA, replacing the more toxic amphotericin B.[3] Other antifungal agents of potential future value in this condition include posaconazole and the echinocandins caspofungin and anidulafungin. Lipid-based formulations of amphotericin B, which are touted as being less toxic than the traditional version, have also seen increasing use. However, for all these antifungals, data on treating IA in ICU patients are exceedingly sparse, and for multiple reasons the response rates in such patients would be expected to be less favorable than in most of those included in clinical trials to date.

COMMENTARY

With ever-increasing availability of new immunosuppressive drugs, along with improvements in life support and other aspects of ICU care, clinicians can expect to encounter IA more and more frequently in critically ill patients. As this thorough review by Meersseman et al demonstrates, diagnosis and treatment of IA in patients who are not in the classic high-risk groups are especially challenging. *Table 2* summarizes current information about approaching the possible diagnosis of IA in critically ill patients.

The relative likelihood of this infection is much greater in certain patient categories than others, and fortunately the diagnosis is often easier to confirm in them than in the larger numbers of patients at lower yet still important risk. Neither positive nor negative findings on chest imaging, stains and cultures of respiratory tract specimens, and serum tests can be considered definitive, and the clinician is faced with synthesizing complex and sometimes contradictory results in attempting to diagnose IA. In most instances, definitive diagnosis continues to require histologic demonstration of tissue invasion. ■

Table 2:
Relative Clinical Value of Available Diagnostic Methods for Invasive Aspergillosis in ICU Patients

Relative risk for invasive aspergillosis	High	Lower
Clinical setting	Neutropenia (<500 neutrophils/mL) Hematologic malignancy Allogenic bone marrow transplant	Prolonged corticosteroid therapy Other immunosuppressive therapy COPD Cirrhosis (especially w/ICU stay >7 days) HIV infection Solid organ transplant Solid organ cancer
Relative likelihood of establishing diagnosis		
Lung biopsy showing branching, septated hyphae	++++	++++
(+) Culture	+++	++
Direct microscopy on BALF	+++	++
Galactomannan*	+++	??
PCR	+++	??
β-^{1,3}D-glucan	++	??
Halo sign or crescent sign on chest CT scan	++	+

* Positive test may be more specific on BALF than on serum

BALF, bronchoalveolar lavage fluid; BM, bone marrow; COPD, chronic obstructive pulmonary disease; CT, computed tomography; PCR, polymerase chain reaction test for detection of circulating fungal DNA

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Special Feature

Nutritional Support for the Acutely Critically Ill Patient

By Saadia R. Akhtar MD, MSc

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Dr. Akhtar reports no financial relationship to this field of study.

Although it is understood that good nutrition is essential for normal immune function, wound healing and maintenance of muscle mass and function, and is likely beneficial for overall recovery from the highly catabolic state of acute critical illness, it is less clear when and how best to deliver adequate nutritional support in practice. Availability of robust data is limited for a variety of reasons. It would be unethical to compare nutrition to no nutrition, and thus such a study has never been done. Furthermore, intensive care unit patients are generally quite heterogeneous in terms of, for instance, admitting diagnoses, severity of illness, co-morbidities and baseline nutritional status. This makes it challenging to design studies and enroll enough subjects within subgroups to achieve the power necessary to evaluate important clinical outcomes. It may also make comparison between studies unfeasible.

Nevertheless, several scientific organizations have developed (often differing) practice guidelines and position papers on nutrition in the ICU: the American College of Chest Physicians, American Society for Parenteral and Enteral Nutrition, Canadian Critical Care Clinical Practice Guidelines Committee, and European Society for Clinical Nutrition and Metabolism, to name just a few.[1] Using such statements and recent literature, this brief report will provide an overview of the issues relating to nutritional support for the acutely critically ill patient.

How Much Nutrition Should Be Provided?

The total energy expenditure and caloric requirements of critically ill patients vary greatly, based on their specific illness (for example, caloric needs may be much higher for a patient with septic shock compared to one with a head injury) as well as time spent in the hospital. It is clear that there are potential hazards of overfeeding, such as azotemia, hypercarbia, metabolic acidosis, and hyperglycemia. Similarly, there are risks of severe underfeeding, such as increased infections and mortality. Some authors favor mild to moderate hypocaloric nutrition to avoid the risks of overfeeding; however, there are no data to support or negate this recommendation.[2]

An estimated total energy expenditure of about 25 ± 5 kcal/kg/day is a widely accepted starting point.[3] It is suggested that this be provided with about 1.5g/kg/day protein, ≤ 6g/kg/day carbohydrates, and ≤ 2.5kg/day lipids.[1] Indirect calorimetry may be used to guide nutritional support, particularly if there are clinical signs concerning for over- or under-feeding. However, there is no specific evidence for or against its utility.

Only 1 study has evaluated the starting volume of enteral feedings.[4] Eighty-two patients with head injury were randomized to receive feedings at their goal rate immediately or advance gradually. The former was associated with improved neurological outcomes and decreased infection risk.

What is the Best Route of Administration?

While some debate remains over the benefits, risks, and respective roles of enteral vs parenteral nutrition for acutely critically ill patients, most studies, experts and current practice guidelines recommend the enteral route as the first choice. Enteral nutrition maintains gastrointestinal integrity,[5] while parenteral nutrition is clearly associated with gut mucosal atrophy, bacterial translocation, and increased risk of infection. (It is important to note that the risk of infection with parenteral nutrition cannot be fully explained by hyperglycemia.[6])

Especially if poorly tolerated, with high gastric residuals, enteral nutrition may increase the risk of hospital- and ventilator-associated pneumonia, and also prolong mechanical ventilation and ICU stays.[7] However, these risks can be reduced by elevation of the head of the bed.[8] Although advocated by some, the utility of small bowel feeding for decreasing risk of nosocomial pneumonia when compared to gastric feeding remains unclear.[9,10]

One meta-analysis evaluated 13 randomized studies comparing enteral to parenteral nutrition in mechanically ventilated critically ill patients. Relative risk for any infection was 0.61 for patients receiving enteral nutrition.[11] These results were replicated in a second systematic review.[12]

Overfeeding and hyperglycemia are also potential concerns, particularly with parenteral nutrition. Hyperglycemia is less a concern today with the use of intensive insulin drip protocols.[13] It is of interest that enteral nutrition often unintentionally provides hypocaloric feeding, at least initially: several observational studies and surveys have shown that generally only about 50-60% of the target is achieved in the first few days of enteral feeding.[14] Withholding lipids with

parenteral nutrition or providing hypocaloric parenteral nutrition may decrease infection risk and improve other outcomes as well.[15]

Finally, according to available evidence, there is no difference in outcomes between using enteral nutrition alone and combining enteral and parenteral nutrition.[11]

When Should Nutrition be Started?

In the past, enteral feeding was often not initiated until day 5-7 of critical illness. The arguments supporting this included the common occurrence of gastroparesis and decreased bowel motility in acute illness and the presence of "adequate" stores in previously healthy patients. Over time it has become clear that not only does small bowel function remain intact, but lack of feeding may lead to villous atrophy, loss of gastrointestinal integrity and increased bacterial translocation. Multiple animal studies confirm that early enteral feeding reduces markers of ischemic/oxidative injury in various organs, improves gastrointestinal blood flow, decreases bacterial translocation from the gut and even improves wound healing.

The benefits of early enteral feeding have been demonstrated in human clinical trials as well. A 2001 meta-analysis of 15 randomized controlled trials (with 753 patients) compared early (within 36 hours of admission or surgery) to late enteral nutrition in acutely ill patients (post-surgical, head injured, burn and medical ICU).[16] Although there was considerable heterogeneity between the studies, infection risk and length of stay were significantly reduced in the early enteral nutrition group (19% vs 41% and mean reduction of 2 days, respectively). There were non-significant trends towards lower risk of non-infectious complications and death as well. Heyland et al's 2003 meta-analysis of 8 trials (including 4 studies not considered by the 2001 work) comparing early (within 48 hours of admission to an intensive care unit) to late enteral feeding arrived at similar results.[11]

Does the Specific Composition of the Nutritional Support Matter?

Enteral feeding formulas with a variety of additives with potential for immune modulation are available. These additives include arginine, glutamine, omega-3 fatty acids, antioxidants, fiber, and others. There have been several studies of such immunonutrition, without consistent evidence of benefit.[3, 11] The largest randomized controlled trial of a formula containing several of these additives evaluated 597 mixed surgical and medical intensive care unit patients and found no differences in infections, lengths of stay or mortality.[17]

One randomized controlled study compared Oxepa® (enteral formula containing fish oil and antioxidants) to a standard formula in patients with ARDS. Those patients receiving Oxepa® had reduced ventilator time, intensive care unit length of stay and organ failures: there was a non-significant trend towards reduced mortality.[18] This feeding formula has also been studied in patients with severe sepsis and septic shock with similar results.[19] Both of these studies have been criticized for using a potentially pro-inflammatory, high fat control formula. Furthermore, because Oxepa® contains a variety of substances that may impact the inflammatory response, it is difficult to know which component led to benefit.

Glutamine has been shown to reduce infections, improve wound healing and possibly improve mortality in small studies of trauma and burn patients. This has been demonstrated with glutamine supplementation to parenteral nutrition as well. Glutamine supplementation for larger, heterogeneous intensive care unit populations, however, imparts no benefit.[11]

Pre-, pro- and synbiotics added to enteral formulations for nutritional support of critically ill patients do not appear to impact clinical outcomes.[20]

Finally, no outcome differences have been demonstrated for alimental vs whole-protein feeding formulas in critically ill patients. (The former may be associated with increased diarrhea and are certainly appropriate for patients with chronic malabsorption/GI disease such as short bowel syndrome, chronic pancreatitis or other.)[11]

Recommendations

Limited data suggest that nutritional support should be initiated for all critically ill patients within 24-48 hours of admission. The enteral route is preferred and should be maximally pursued (with use of pro-motility agents or small bowel feeding tubes if needed). Parenteral nutrition should be reserved for those patients unable to receive/tolerate enteral feeds (for instance, bowel obstruction, bowel ischemia, severe ileus). Intensive glucose control should be implemented and patients carefully monitored to avoid over- or severe under-feeding. Consideration could be given to adding glutamine for trauma and burn patients and using Oxepa® for patients with ARDS or septic shock. Finally, protocols and algorithms may facilitate initiation of nutrition in critical care settings and improve clinical outcomes.[21] ■

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How Often Are ICU Chest Tubes Malpositioned?

ABSTRACT & COMMENTARY

By David J. Pierson, MD, Editor

Synopsis: *In this study of surgical ICU patients in whom chest tubes were placed percutaneously for pneumothorax or sterile pleural effusion, 21% of the tubes were found on chest CT to be in a fissure, and another 9% were intraparenchymal. Only a minority of the malpositions were described in the official radiology reports.*

Source: Remerand F, et al. *Anesthesiology.* 2007;106:1112-1119.

In this study from a surgical ICU in Paris, the investigators prospectively gathered data on chest tubes percutaneously inserted in consecutive critically ill patients. After the presence of pleural fluid or air was determined using bedside thoracic ultrasound, chest tubes were inserted either by blunt dissection or using a trochar by senior physicians, residents, or medical students under direct supervision by senior staff. Bedside chest radiographs were taken after insertion to screen for obvious malposition such as kinking or new parenchymal density around the tube. When patients with chest tubes subsequently underwent CT scanning for separate clinical indications (not part of the study), the authors used a special protocolized method for determining the position of the tubes, in an attempt to determine the incidence of previously unsuspected malposition.

During the period of the study, 122 chest tubes were inserted in 75 patients with pneumothoraces or sterile pleural effusions. Of these, 63 patients with 106 tubes also had a chest CT scan. The mean interval between chest tube insertion and CT scanning was 3.5 ± 2.9 days. In all, 32 (30%) of the chest tubes were determined to be malpositioned—22 (21%) in a fissure and 10 (9%) intraparenchymal. Two additional tubes had proximal drainage holes outside the pleural space, and one tube was believed to be inside the chest but extrapleural. In none of the instances of tube malposition was this suspected on the basis of the standard chest radiograph.

In 103 of the 106 instances, the radiologists officially reading the chest CT scans were unaware of the study and the protocol used for determining chest tube position. Of the 9 intraparenchymal tubes in this group, only 2 were correctly diagnosed; 4 were reported to be in correct position and 3 were not described. Overall, the sensitivity, specificity, and negative and positive predictive values of the radiologists' reports in detecting malpositioned chest tubes were 23%, 49%, 63%, and 18%, respectively.

Use of a trochar during insertion was associated with a higher incidence of tube malposition ($p = 0.032$). Operator experience and level of training were not related to the incidence of this complication. One patient with an intraparenchymal tube developed a bronchopleural fistula, associated with lung abscess, empyema, and septic shock. Three intraparenchymal and 2 intrafissural tubes were inefficient in draining the pleural fluid or air and required additional procedures—new tubes in 4 patients and thoracotomy in one. No other observed clinical outcomes were different in patients with correctly placed vs malpositioned chest tubes.

COMMENTARY

Malpositioning of chest tubes inserted percutaneously in critically ill patients is common, and is missed frequently by both clinicians and radiologists. The CT scans used for determining malposition in this study were not

obtained specifically for that purpose, and as the authors point out, the radiologists were likely focusing on the clinical indications for which the scans had been ordered. Nonetheless, given the potential clinical importance of incorrect positioning, it is discouraging to note that it was missed on the official readings most of the time.

The adverse effects of malpositioned chest tubes include ineffective drainage of the fluid or air for which they were placed, along with more serious complications such as bronchopleural fistula, abscess formation, and life-threatening bleeding. Thus, increased efforts to identify tube malpositioning when it occurs would seem worthwhile, particularly when a recently-placed chest tube does not function as intended. Radiologists who interpret chest CT scans should be asked to comment on the course and location of chest tubes, even when the study is obtained for other reasons. ■

CME / CNE Questions

30. Which of the following BNP levels has the highest sensitivity and positive predictive value for the diagnosis of ARDS in patients with hypoxemic respiratory failure?
a. 80 pg/ml
b. 120 pg/ml
c. 200 pg/ml
d. 500 pg/ml
e. 1200 pg/ml

31. Regarding the use of the BNP assay in patients with dyspnea or hypoxemic respiratory failure, which of the following statements is true?
a. The BNP level cannot distinguish between pulmonary and cardiac causes of dyspnea in the emergency department.
b. The BNP level can be used as a surrogate marker for the pulmonary capillary wedge pressure in the ICU
c. A BNP level below 200 pg/ml is not consistent with a diagnosis of ARDS
d. A BNP level above 1200 pg/ml is consistent with a diagnosis of cardiogenic pulmonary edema.
e. In ARDS and cardiogenic pulmonary edema patients, lower BNP levels are associated with higher mortality

32. Which of the following patient categories places them at highest risk for invasive aspergillosis?
a. Prolonged treatment with corticosteroids
b. Cirrhosis
c. COPD
d. Neutropenia (<500 cells/mL)
e. HIV infection

33. Which of the following has the highest sensitivity and specificity in diagnosing invasive aspergillosis?
a. Direct microscopy on bronchoalveolar lavage fluid
b. Positive culture from endotracheal suction specimen
c. Serum galactomannan
d. Serum PCR for fungal DNA
e. Transbronchial lung biopsy showing branching, septated hyphae

34. What proportion of chest tubes that appeared to be in correct position by standard chest X-ray were found to be either intrafissural or intraparenchymal on chest CT?
a. 5%
b. 10%
c. 20%
d. 30%
e. 40%

35. Which of the following factors was associated with an increased incidence of chest tube malposition?
a. Use of a trochar instead of blunt dissection during placement
b. The operator having performed fewer previous tube thoracostomies
c. The operator being a resident vs an attending physician
d. All of the above
e. None of the above

Answers: 30(c); 31(d); 32(d); 33(e); 34(d); 35(a)

CME / CE Objectives

After reading each issue of *Critical Care Alert*, readers will be able to do the following:

- Identify the particular clinical, legal, or scientific issues related to critical care.
- Describe how those issues affect nurses, health care workers, hospitals, or the health care industry in general.
- Cite solutions to the problems associated with those issues.

In Future Issues:

Effects of Delayed Transfer to ICU

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Stopping Statins in At-Risk Patients — Just Too Risky

In this issue: *Make sure your patients don't stop statins after a stroke or surgery; MRSA is becoming more resistant to mupirocin; new asthma treatment guidelines; and FDA approvals and warnings.*

Stopping statins, even briefly, after stroke or cardiovascular surgery increases vascular complications according to 3 new studies. Spanish investigators looked at 89 patients who were on chronic statin therapy and were admitted with acute stroke. Half were randomized to statin withdrawal for the first 3 days after admission, while the other half immediately received atorvastatin 20 mg/day. After 4 days, the statin withdrawal group was also started on atorvastatin. The primary outcome was death or dependence after 3 months as defined by modified Rankin scale of 2 or more. After 3 months, 60% of those in the statin withdraw group were disabled to the point of dependence compared with 39% of those that continued statin therapy (P = 0.043). Early neurologic deterioration was also far greater in the statin withdrawal group (65.2% versus 20.9%; $P < 0.0001$). Statin withdrawal patients also had greater infarct volume (P = 0.002). The authors conclude that statin withdrawal in the first few days after stroke is associated with a markedly increased risk of death or dependency at 90 days; hence, treatment should continue the acute phase of an ischemic stroke (*Neurology* 2007; 69:904-910).

In another study, researchers in Italy looked at stroke patients who discontinued statins after discharge from the hospital. The study population included 631 stroke patients (322 men, 309 women) without evidence of heart disease. All patients were discharged on a statin, but 38.9% discontinued the drug within 12 months. In the 12 months of follow-up, 116 patients died. After adjustment for all confounders and interactions, the hazard ratio for mortality in patients who quit a statin was 2.78 (95%CI, 1.96-3.72; P = 0.003) or nearly 3 times higher risk of death (*Stroke* 2007, published online ahead of print 8/30/07).

Another study from the Netherlands looked at a brief interruption in statin therapy associated with major vascular surgery. Nearly 300 patients on statins underwent major vascular surgery, and statin therapy was interrupted in the perioperative period in 70 patients for mean duration of 3 days. An association was observed between statin discontinuation and an increase risk of postoperative troponin release (HR 4.6) and the combination of MI and cardiovascular death combined (HR 7.5). Because many surgical patients are NPO and unable to take oral statins, and there's no intravenous statin available, the only extended release statin was tried on a subset of patients preoperatively. Patients receiving extended-release fluvastatin had fewer perioperative cardiac events compared to other statins (*Am J Cardiol* 2007; 100:316-320). The message of these studies is that statin interruption, even for a brief period during hospitalization, may lead to serious adverse events in patients at risk.

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Mupirocin Less Effective Against MRSA

Mupirocin (Bactroban) is becoming less and less effective against MRSA, even in hospitals with low levels of mupirocin use. Researchers from Washington University in St. Louis performed nasal swab cultures for MRSA in all patients admitted to their surgical intensive care unit (SICU) on admission, weekly during hospitalization, and at discharge. Of the 302 positive MRSA isolates, 13.2% were resistant to mupirocin, with 8.6% having high-level resistance. Patients with mupirocin-resistant MRSA were more likely to be older, have a history of a previous admission in last year, and had higher in-hospital mortality. The authors conclude that patients carrying mupirocin-resistant MRSA acquired it through contact with the health-care system; the strains were probably not acquired in the SICU (*Clin Infect Dis* 2007; 45:541-547). Mupirocin is commonly used to decolonize patients who are *staph aureus* carriers or have nasal colonization with MRSA. With resistance patterns increasing nationwide, this strategy may need to change.

New Guideline for Asthma Diagnosis/Management

The National Asthma Education and Prevention Program has issued an update to their clinical practice guidelines for diagnosis and management of asthma (Expert Panel Report 3 [EPR-3]). The new guideline emphasizes the importance of asthma control and highlights 4 areas of emphasis including assessment and monitoring, patient education, control of environmental factors and other asthma triggers, and pharmacotherapy. The new guideline recommends continued use of a stepwise approach to asthma control in which medication doses or types are stepped up or down as needed based on asthma control. Recommendations now are based on 3 age groups, 0-4 years, 5-11 years (a new category), and 12 years and older.. The new age group was added because of evidence that children respond differently to medications than adults. The entire guideline can be found at: http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.pdf .

FDA Actions

The FDA announced on August 14 that manufacturers of rosiglitazone (Avandia) pioglitazone (Actos), and other combination medications containing the 2 drugs will be required to add a "black box" warning to their labeling to reflect the risk of heart failure associated with the 2 drugs. Both drugs have been associated with reports of significant weight gain and edema, and some cases continuation of therapy has lead to poor outcomes including death. The black box warning advises health-care professionals to carefully observe patients taking these drugs for signs and symptoms of heart failure including rapid weight gain, shortness of breath, edema. The warning also recommends not starting either drug in patients with a history of congestive heart failure. The agency continues to review rosiglitazone for the possible increase risk of myocardial infarction associated with use of the drug.

The FDA has approved a new indication for zoledronic acid (Reclast) as a once-a-year treatment for postmenopausal osteoporosis. Reclast is administered as an annual 15-minute intravenous infusion. The drug is a bisphosphonate similar to oral bisphosphonates such as alendronate and risedronate.

Anesiva has received approval to market lidocaine topical powder intradermal injection system (Zingo) to provide local analgesic prior to venipuncture or peripheral intravenous cannulation in children ages 3-18. Zingo is a single-use helium powered system that is administered 1-3 minutes prior to needle insertion. The system is also being studied in trials of adults.

The FDA has approved a new combination of carbidopa, levodopa, entacapone (50 mg/200 mg/200 mg) for the treatment of Parkinson's disease. The new preparation helps reduce the pill burden for Parkinson's patients on multiple medications. Carbidopa/levodopa/entacapone will be marketed by Orion Corporation as Stalevo.

Omrix Biopharmaceuticals has received approval to market human thrombin (Evithrom) to promote blood clotting and control bleeding during surgery. Evithrom is the first human thrombin approved since 1954 and the only product currently available for this indication. It is applied to the surface of bleeding tissue during surgery and may be used in conjunction with absorbable gelatin sponge. Other thrombins currently on the market are derived from cattle plasma.

Nursing mothers who were taking codeine may put their babies at risk of morphine overdose if they are "ultra-rapid metabolizers of codeine," a condition that may affect up to 28% of the population. Codeine is generally recommended for nursing mothers as a cough suppressant and pain medication; however, ultra-rapid metabolizers quickly convert codeine to morphine and excrete it in breast milk. At least one infant death has been associated with this condition. The FDA has issued warning regarding codeine use by nursing mothers, recommending that mothers observe their infants closely while taking the medication for signs of morphine overdose including sleepiness, difficulty breast feeding, breathing difficulties or limpness. ■