

# Critical Care [ALERT]

Authoritative, evidence-based summaries for the critical care clinician

## ABSTRACT & COMMENTARY

### Vitamin C, Thiamine, and Hydrocortisone for Septic Shock

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Dr. Nadler reports no financial relationships relevant to this field of study.

**SYNOPSIS:** The combination of vitamin C, thiamine, and hydrocortisone did not improve outcomes compared with hydrocortisone alone in patients with septic shock.

**SOURCE:** Fujii T, Luethi N, Young PJ, et al. Effect of vitamin C, hydrocortisone, and thiamine vs hydrocortisone alone on time alive and free of vasopressor support among patients with septic shock: The VITAMINS Randomized Clinical Trial. *JAMA* 2020;323:423-431.

Since the retrospective before-and-after study by Marik et al, there has been much discussion about the benefits of the combination of hydrocortisone, vitamin C, and thiamine in patients with septic shock.<sup>1</sup> That trial demonstrated a remarkable decrease in mortality from 40.4% to 8.5% with these interventions. However, the magnitude of the effect and the retrospective, single-center study design raised concerns. The VITAMINS study was a prospective, randomized, open-label, multicenter trial that evaluated the combination of these three medications for the treatment of septic

shock. Patients were included if they were admitted with a primary diagnosis of septic shock with diagnostic criteria of Sepsis-3 fulfilled within 24 hours.<sup>2</sup> Exclusion criteria included age younger than 18 years, patients with do-not-resuscitate orders or with imminent death, contraindications to the study medications, or another need for hydrocortisone. The primary outcome was time alive and free of vasopressors up to day 7. Secondary outcomes included mortality, ventilator-free days, need for renal replacement therapy, length of stay (LOS), and change in Sequential Organ Failure Assessment

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(SOFA) scores. The study was designed to have a 90% power to detect a 25-hour difference of vasopressor-free hours.

The VITAMINS study randomized 216 patients to the combination of vitamin C (1.5 g intravenous [IV] every six hours), hydrocortisone (50 mg IV every six hours), and thiamine (200 mg IV every 12 hours) vs. hydrocortisone alone. Study medications were continued until vasopressor requirements ceased up to 10 days or death occurred. There was no difference in the primary outcome of time alive and free of vasopressors between the intervention and control arms (122.1 vs. 124.6 hours, respectively;  $P = 0.83$ ). Similarly, there was no difference noted in any mortality metric or the overall incidence of death (hazard ratio [HR], 1.18; 95% confidence interval [CI], 0.69-2.01;  $P = 0.54$ ). The two groups also had similar ventilator-free days, renal replacement therapy (RRT)-free days, intensive care unit (ICU)-free days, and overall hospital LOS.

## ■ COMMENTARY

Why might the VITAMINS study results be so different from the previous study by Marik? The duration of vasopressor need in the control and intervention groups in the VITAMINS study was 43.4 and 45.9 hours, respectively, compared with 54.9 and 18.3 hours in the Marik study. Hospital mortality was 20.4% and 23.4% in the VITAMINS control and intervention groups, compared with 40.4% and 8.5%, respectively, in the Marik study. The medication doses in the two trials were identical, although the VITAMINS protocol ended at 10 days while the Marik study continued until ICU discharge.

The study populations had similar SOFA scores (8.3 and 8.7 in the Marik study, compared with 8.4 and 8.6 in VITAMINS in the control and treatment arms, respectively). The VITAMINS study population had slightly higher rates of mechanical ventilation and vasopressor needs. The need for RRT in the VITAMINS study and the treatment arm of the Marik study were similar, although the control arm of the Marik study had a higher rate of RRT. Thus, neither the

population nor the intervention accounts for the difference in outcomes.

The primary differences between these two trials are the strength of the study design and the use of hydrocortisone in the control arm. Specifically, the Marik trial was a before-and-after, single-center study. The interventions occurred during different seasons, with the control group assessed June 2015 through December 2015 and the intervention group assessed January 2016 through June 2016. Although the Marik study used a propensity score adjustment to attempt to control for these factors, this study design is inherently vulnerable to confounding factors.

In contrast, the VITAMINS study was randomized with concurrent control and intervention groups conducted in multiple centers, which is a stronger design. It has been noted before in the Marik study that the mortality rate in the control group was unusually high, while in the intervention group it was surprisingly low. The Marik study also left the use of hydrocortisone in the control group to the discretion of the treatment team, while the VITAMINS study mandated steroids in the control group.

The VITAMINS study failed to demonstrate clinical improvement in patients with septic shock who were treated with vitamin C, thiamine, and hydrocortisone. Although other studies are likely to be performed, this study provides strong evidence against a benefit of these therapies for septic shock. While there is no clear harm to this combination of medications, it seems wiser to focus our efforts on the other, more evidence-based interventions important for sepsis care. ■

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# Impact of Intensive Care Unit Personnel Decisions and Staffing on Patient Outcomes

By Drayton Hammond, PharmD, MBA, BCPS, BCCCP

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Dr. Hammond reports no financial relationships relevant to this field of study.

**SYNOPSIS:** Nurses with relatively high autonomy alongside a dedicated intensive care unit (ICU) clinical pharmacist and 24/7 intensivist coverage were associated with the lowest hospital mortality and shortest ICU lengths of stay and mechanical ventilator durations compared to other staffing models.

**SOURCE:** Zampieri FG, Salluh JIF, Azevedo LCP, et al. ICU staffing feature phenotypes and their relationship with patients' outcomes: An unsupervised machine learning analysis. *Intensive Care Med* 2019;45:1599-1607.

The complexity of providing excellent care for critically ill patients continues to increase alongside advances in technology, changing organizational factors in healthcare, and a consistent stream of published literature. Although the proper distribution of intensivists to patients throughout a day remains an area of study,<sup>1,2</sup> the presence and autonomy of support staff (e.g., pharmacists, nurses, and respiratory therapists) has become an area of interest for most intensive care units (ICUs). The investigators of the ORganizational CHaracteriSTics in cRITICAL cAre (ORCHESTRA) study evaluated whether ICU staffing features were associated with improved patient outcomes using cluster analysis directed by machine learning.<sup>3</sup>

The ORCHESTRA investigators performed a retrospective analysis of prospectively collected data on consecutive adults admitted to 93 medical-surgical ICUs in Brazil during 2014-2015 to determine clinical outcomes.<sup>3</sup> Additionally, cross-sectional surveys and interviews of ICU directors and/or chief nurses were performed to elicit the presence and extent to which hospital and ICU organizational, structural, and process characteristics were available and used. Nonphysician staff members' autonomy was assessed using surveys (seven items, with scores ranging from 0 [low] to 14 [high]). Three ICU clusters were developed based on ICU characteristics. The defining characteristics of each cluster were: no board-certified intensivist in the ICU 24/7, no dedicated ICU pharmacist, and low nurse autonomy score (Cluster 1); no board-certified intensivist in the ICU 24/7, dedicated ICU pharmacist, and moderate nurse autonomy score (Cluster 2); and board-certified intensivist in the ICU 24/7, dedicated ICU pharmacist, and high nurse autonomy score (Cluster 3). The best patient outcomes were observed

in Cluster 3: lower adjusted hospital mortality (odds ratio, 0.92; 95% confidence interval [CI], 0.87-0.98), shorter ICU length of stay (subhazard ratio, 1.24; 95% CI, 1.22-1.26), and shorter mechanical ventilation duration (subhazard ratio, 1.61; 95% CI, 1.54-1.69). The worst outcomes were observed in Cluster 1.

## ■ COMMENTARY

The investigators described the impact of combinations of various organizational and personnel factors rather than the isolated effects from a specific, singular variable. In other studies, researchers have observed improved outcomes with nurse-led interventions, including improved mechanical ventilator weaning, minimization of sedation with better patient comfort, earlier goal enteral feeding, and a greater culture of safety.<sup>4-7</sup>

In this study, the mean nursing autonomy score was 9.62 (out of 14), which suggests that many opportunities still exist for increased nursing autonomy and potentially improved patient outcomes. However, nursing leadership must be supported by physician collaboration and adequate education. Similarly, improved patient outcomes and avoidance of healthcare costs have been realized with dedicated ICU clinical pharmacists.<sup>8-10</sup> Whereas an ideal patient-to-nurse ratio in the ICU of 1:2 has been established, the ideal pharmacist-to-patient ratio in the ICU remains controversial, with 1:12 to 1:28.<sup>11</sup> This study suggests there should be a dedicated ICU pharmacist for each clinical service providing ICU-level care to support that team's efforts to improve patient outcomes. Lastly, the importance of intensivist coverage alongside these other personnel decisions is paramount. The complement of healthcare professionals in Cluster 3 represents a

desirable and achievable staffing model that has been shown to improve patient outcomes. ■

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## ABSTRACT & COMMENTARY

# Maximal Lung Recruitment Strategy Does Not Reduce Ventilator-Free Days in the Setting of Acute Respiratory Distress Syndrome

By *Vibhu Sharma, MD, MS*

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Dr. Sharma reports no financial relationships relevant to this field of study.

**SYNOPSIS:** In this randomized trial, daily maximal recruitment trials failed to reduce ventilator-free days in the setting of acute respiratory distress syndrome, but increased the risk of cardiovascular adverse effects.

**SOURCE:** Hodgson CL, Cooper DJ, Arabi Y, et al. Maximal recruitment open lung ventilation in acute respiratory distress syndrome (PHARLAP). A phase II, multicenter randomized controlled clinical trial. *Am J Respir Crit Care Med* 2019;200:1363-1372.

**T**he Permissive Hypercapnia, Alveolar Recruitment, and Low Airway Pressure (PHARLAP) trial recruited patients with moderate to severe acute respiratory distress syndrome (ARDS) (PaO<sub>2</sub>/FiO<sub>2</sub> [or P/F] ratio of < 200 with a positive end-expiratory pressure [PEEP] > 5 cm H<sub>2</sub>O). Patients had to be mechanically ventilated for < 72 hours and diagnosed with ARDS using the Berlin criteria. Patients were randomized in a 1:1 ratio to the PHARLAP intervention or the control strategy of low tidal volume (V<sub>t</sub>) per ARDSNet criteria (the PHARLAP intervention is described subsequently). Patients were stratified by site and the etiology of ARDS (pulmonary vs. extrapulmonary).

The PHARLAP intervention consisted of a pressure control (PC) mode with an inspiratory pressure of 15 ± 3 cm H<sub>2</sub>O targeting a V<sub>t</sub> of 4 mL to 6 mL and a plateau pressure maintained at < 28 cm H<sub>2</sub>O whenever possible. Permissive hypercapnia was allowed. Daily recruitment maneuvers (RMs) were performed (for up to five days) in the PHARLAP intervention group. The protocol for the RMs consisted of two separate recruitment maneuvers: a staircase recruitment maneuver (SRM) and then a brief recruitment maneuver (BRM), if needed. The first step, SRM, involved increasing PEEP to 20 cm H<sub>2</sub>O all the way up to 40 cm H<sub>2</sub>O pressure, in 10 cm H<sub>2</sub>O increments, with two-minute plateaus

at each step. A high pressure of 55 cm H<sub>2</sub>O thus was possible. Hemodynamic instability or marked oxygen desaturation (SpO<sub>2</sub> < 85%) were criteria for termination of the PEEP titration maneuver, with the PEEP left at the level prior to the one at which desaturation or hemodynamic instability happened. After completion of the stepwise increase to maximal tolerated PEEP, the PEEP was reduced immediately to 25 cm H<sub>2</sub>O and subsequently reduced in 2.5 cm H<sub>2</sub>O decrements every three minutes until a PEEP of 15 was reached or desaturation (SpO<sub>2</sub> drop of ≥ 2%) occurred. The point at which desaturation occurred was deemed the derecruitment PEEP. If derecruitment occurred, a second recruitment maneuver (BRM) was performed in the pressure control mode with the inspiratory pressure set at 15 ± 3 cm H<sub>2</sub>O and PEEP set at the maximal tolerated PEEP during the SRM for two minutes. PEEP then was returned to 2.5 cm H<sub>2</sub>O above derecruitment PEEP.

In the PHARLAP intervention group, after the RMs (“open lung procedure”) were performed, the PC level was reduced to achieve total pressure (PEEP + PC) to < 28 cm H<sub>2</sub>O using reductions in targeted V<sub>t</sub> to as low as 4 mL/kg as needed. Failure of the recruitment strategies and persistent severe hypoxemia allowed for intervention with rescue strategies (e.g., high-frequency oscillatory ventilation, inhaled nitric oxide [iNO] or prostacyclin, prone positioning, or extracorporeal membrane oxygenation [ECMO]). The control group was ventilated using low V<sub>t</sub> strategies per ARDSNet criteria, and rescue strategies as noted earlier were implemented as needed and as available by site.

Most patients recruited had pulmonary ARDS. The mean PEEP and P/F ratios were higher in the PHARLAP group, and pH was lower compared to the control group. Importantly, from day 1 to day 4 of 5 of the PHARLAP intervention, plateau pressures were significantly higher in the PHARLAP group (though still < 28 cm H<sub>2</sub>O), while driving pressures were not better than the control group beyond day 1. At 28 days, the number of ventilator-free days in the PHARLAP group was not different from the control group.

This study did not find differences in the rates of pneumothorax or mortality. However, the patients randomized to the PHARLAP group did have a reduction in the use of iNO, the need for ECMO, and prone positioning. There were no differences in the proportion of patients on neuromuscular blockade between groups. The PHARLAP strategy was associated with an increase in the risk of cardiac arrhythmias (atrial fibrillation, ventricular tachycardia, and ventricular fibrillation). The trial

was terminated prematurely because of “safety concerns and perceived loss of equipoise at the sites” after publication of the Alveolar Recruitment Trial (ART). This resulted in recruitment cessation at 114 patients instead of the originally planned 340, resulting in an underpowered study for the primary endpoint.

#### ■ COMMENTARY

This trial attempted to revisit the “open lung strategy” in the setting of ARDS, wherein attempts are made to open collapsed alveoli by RMs that transiently increase mean airway pressure up to (and occasionally above) 40 cm H<sub>2</sub>O. This trial had to be terminated early after publication of another trial (Alveolar Recruitment Trial)<sup>1</sup> that showed an increase in cardiovascular adverse effects, barotrauma, and mortality at 28 days with RMs. A meta-analysis of other trials involving RMs and including the patients in this trial performed by the authors suggested no increase in mortality. However, an increased risk of barotrauma persisted. A plateau pressure of < 30 cm H<sub>2</sub>O is the major determinant of mortality, with lower plateau pressures (even those below 30 cm H<sub>2</sub>O) associated with decreasing mortality. The intervention group in this trial had a plateau pressure higher than the control group for each of the four out of five days (the duration that RMs were performed). Although plateau pressure remained below 30 cm H<sub>2</sub>O in the intervention group, lower plateau pressures were achieved in the control group with a simple low V<sub>t</sub> strategy, and the differences were significant. The RMs were performed by expert clinicians who were “senior medical staff” and took an average of 18 minutes in my estimation. The authors stated that “the time required at the bedside limited recruitment into the study.” While oxygenation indices were better in the intervention group, oxygenation does not predict mortality in the setting of ARDS.

Prone positioning is an intervention that has a demonstrable mortality benefit, especially when done early in the setting of severe ARDS.<sup>2</sup> A recent trial also seemed to suggest a mortality benefit for early use of airway pressure release ventilation (APRV) as a mechanical ventilation strategy in the setting of severe ARDS.<sup>3</sup> Animal studies<sup>4</sup> suggest a more prolonged benefit of RMs performed while prone, and other smaller clinical studies<sup>5,6</sup> suggest a larger benefit for RMs in the prone position compared to the supine position. There are no studies that have compared the effects of an RM in the prone vs. the supine position with respect to endpoints studied in the PHARLAP trial. A low V<sub>t</sub> strategy with early proning and possible use of APRV prior to initiating rescue therapies (ECMO/iNO) may be the preferred strategy

for ventilating ARDS patients. The significantly higher plateau pressure in the intervention group in this study (albeit still < 30 cm H<sub>2</sub>O) over the four of five days after randomization is the strongest argument to discard RMs as a routine intervention in moderate to severe ARDS. ■

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## ABSTRACT & COMMENTARY

# Antibiotic Therapy to Reduce the Incidence of Ventilator-Associated Pneumonia After Cardiac Arrest

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Dr. Sharma reports no financial relationships relevant to this field of study.

**SYNOPSIS:** In this prospective, randomized trial, intravenous amoxicillin-clavulanate (dosed three times daily and given for two days) administered to patients admitted with out-of-hospital cardiac arrest due to a shockable rhythm reduced the incidence of early ventilator-associated pneumonia.

**SOURCE:** François B, Cariou A, Clere-Jehl R, et al; CRICS-TRIGGERSEP Network and the ANTHARTIC Study Group. Prevention of early ventilator-associated pneumonia after cardiac arrest. *N Engl J Med* 2019;381:1831-1842.

**T**his prospective, randomized controlled trial assessed whether prophylactic antibiotic therapy with intravenous amoxicillin-clavulanate (IVAC) administered to adult patients undergoing targeted temperature management (TTM) to 32-34°C after out-of-hospital cardiac arrest due to a shockable rhythm would reduce the incidence of ventilator-associated pneumonia (VAP). A total of 1,116 patients were assessed for eligibility, and 198 underwent randomization. Most exclusions were because of either a non-shockable rhythm (30%) or in-hospital cardiac arrest (20%). Other reasons for exclusion included preexisting pneumonia, abnormal chest X-ray at presentation, ongoing antibiotic therapy, witnessed aspiration during initial intubation, moribund status, or ≥ 6 hours between return of spontaneous circulation and randomization. The method of TTM was not standardized, but rapid achievement of hypothermia was required. All patients received a bundle of interventions

to prevent VAP (e.g., head of the bed elevation, daily spontaneous awake trial [SAT], and daily spontaneous breathing trial [SBT]). Patients were randomized to IVAC 1 g or intravenous (IV) placebo three times daily for two days.

The primary endpoint was the incidence of VAP and required clinical criteria, imaging, and microbiological criteria. The Clinical Pulmonary Infection Score (CPIS) was calculated to determine whether VAP was present, with a score > 6 implying a higher probability of VAP. This score incorporates several criteria with points assigned for each: tracheal secretions characterized as rare/abundant/abundant and purulent, chest X-ray findings, fever or hypothermia, white blood cell count, PaO<sub>2</sub>/FiO<sub>2</sub> ratio, radiographic progression, and exclusion of congestive heart failure (CHF) and acute respiratory distress syndrome (ARDS). A CPIS > 6 was required based on these criteria. In addition, two or more

of the following were required: auscultatory findings of pneumonia or consolidation, ventilator changes reflecting worsening ventilation/perfusion (V/Q) mismatch, or worsening PaO<sub>2</sub>/FiO<sub>2</sub> ratio. Radiographic criteria included new or worsening consolidation, and microbiologic criteria included a positive respiratory culture at prespecified thresholds of 10<sup>6</sup> colony forming units (CFU) for endotracheal aspirates and 10<sup>4</sup> CFU for bronchoalveolar lavage (BAL) specimens. The specific sampling technique of the lower respiratory tract was “at the discretion of the attending physician.” Blood cultures were obtained upon suspicion for VAP as well. VAP was defined as early if the occurrence was noted within seven days and late if it occurred after seven days of arrest. A final diagnosis of VAP was based on the clinical, radiologic, and microbiologic criteria, with all information available to a committee composed of two experienced intensivists. In the event of disagreement with respect to the diagnosis, a third intensivist arbitrated the final diagnosis.

The investigators reported 80 cases of VAP; however, the adjudicating committee only reported cases with pathogen documentation (60 of the 80). The initial rate of agreement on a VAP diagnosis among these 60 patients was 78%, requiring an adjudicator in the remaining 22%. Among patients receiving the antibiotic intervention, 33% of the sampled lower respiratory tract secretions grew bacterial pathogens, whereas among those receiving placebo, 62% of the sampled secretions grew pathogenic bacteria. Cases deemed to be “colonization” based on culture results were excluded for analysis by the adjudication committee. IVAC reduced the risk of early VAP but not late VAP, with a hazard ratio (HR) of 0.53 (95% confidence interval [CI], 0.31 to 0.92; *P* = 0.03). There was no difference in ICU length of stay, nonpulmonary secondary infections, or the development of multidrug-resistant organisms out to seven days after treatment with IVAC. Mortality was unaffected by treatment with IVAC.

#### ■ COMMENTARY

Patients undergoing TTM are at increased risk for infections, particularly pneumonia. This is hypothesized to be because of the prolonged activation of NF-κβ and augmented generation of cytokines in the setting of hypothermia.<sup>1</sup> An impaired immune response to gram-negative bacteria after cardiac arrest also has been hypothesized to play a role regardless of body temperature.<sup>2</sup> The patients in this study were a relatively young (median age approximately 60 years), majority male, and presumably community-dwelling group (although this is not specified).

This study demonstrates the difficulty of diagnosing a simple condition for the purposes of a clinical trial. Confirmation of VAP required multiple clinical criteria as detailed earlier, some of which have a questionable interrater reliability (e.g., auscultation). The CPIS is cumbersome to compute and is based on several criteria, some of which are observer-dependent, and, therefore, subjective. Tracheal secretion characteristics and progression of pulmonary opacities are examples. One study found that the specificity of a CPIS > 6 for diagnosing VAP on day 3 was only 47%, with a sensitivity of 89%.<sup>3</sup> The authors of the ANTHARTIC study accepted that, “The diagnosis of VAP remains complex owing to considerable heterogeneity in its definition.” A total of 80 patients were reported by the investigators to have VAP based on several criteria; however, only 60 were diagnosed with VAP by the adjudication committee. The initial rate of agreement by the two adjudicators for these 60 patients was 78%, implying that for 33 of the original 80 patients (41%) diagnosed as VAP by the investigators, the diagnosis was uncertain at best.

This study assumes that all VAP is diagnosed only if microbiologic cultures are positive and at a certain clinical threshold. The microbiologic thresholds as described are not used routinely in clinical practice, and the panel making updated recommendations for hospital-acquired pneumonia (HAP)/VAP in 2016 recommended against using them.<sup>4</sup> Arguably, from a practical perspective, VAP may be diagnosed and treated in the absence of clearly positive microbiological cultures if multiple other clinical criteria point to the diagnosis. Cases with culture results deemed to be “colonization” were excluded from the analysis and were not reported. The flow diagram for the trial documented only one case with colonization excluded prior to randomization, but the number excluded after randomization due to “colonization” was not reported.

With respect to the bacterial pathogens reported, the majority were susceptible to IVAC and, while this may be true of the pathogens in intensive care units (ICUs) in Europe, this may not be true of ICU settings in other parts of the world. About one-third (35%) of all bacteria isolated were those that colonize the upper respiratory tract and included *Haemophilus influenzae*, *Streptococcus pneumoniae*, streptococcal species, *Neisseria* species, and *Moraxella*, suggesting that at least some of these events were simply due to aspiration of upper airway secretions that had not been apparent at the time of enrollment. Most of these pathogens were sensitive to the antibiotic being tested. The authors

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did not report on the number of events (i.e., VAP) diagnosed within the first two days of intubation; these would be classified more typically as community-acquired pneumonia (CAP). The authors also did not report on the proportion of *Staphylococcus aureus* species isolated that were resistant to methicillin. While staphylococci were overrepresented in the control group (14% vs. 9% in the intervention group), the relative proportions of methicillin-resistant *S. aureus* (MRSA) would be important for purposes of determining antibiotic efficacy. Finally, the investigators did not define what the diagnoses were in the 20% of cases deemed not to be VAP.

In summary, while the authors made a valiant attempt to diagnose VAP with high certainty, there were shortcomings. A more pragmatic trial may have been to randomize all 80 patients initially diagnosed with VAP. Until more outcome data are available, it may be prudent to prophylactically treat only those post-arrest comatose patients who are younger and community-dwelling (such as those enrolled in this study) and

those with hypothermia targeted to 33° C rather than targeted normothermia, given some evidence of immunoplegia in the setting of hypothermia. IVAC is not available for use in the United States. Intravenous ampicillin/sulbactam may be a reasonable alternative once consideration has been given to institution/community-specific antibiograms. ■

#### REFERENCES

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#### CME/CE QUESTIONS

1. **The VITAMINS study of hydrocortisone, thiamine, and vitamin C for septic shock demonstrated:**
  - a. no improvement in mortality.
  - b. improvement in vasopressor-free days.
  - c. improvement in renal replacement therapy-free days.
  - d. improvement in hospital length of stay.
2. **In the study by Zampieri et al, which cluster of staffing attributes was associated with the best patient outcomes?**
  - a. No board-certified intensivist in the intensive care unit (ICU) 24/7, no dedicated ICU pharmacist, and low nurse autonomy score
  - b. No board-certified intensivist in the ICU 24/7, dedicated ICU pharmacist, and moderate nurse autonomy score
  - c. Board-certified intensivist in the ICU 24/7, no dedicated ICU pharmacist, and moderate nurse autonomy score
  - d. Board-certified intensivist in the ICU 24/7, dedicated ICU pharmacist, and high nurse autonomy score
3. **Which of following best describes the initial recruitment maneuver in the PHARLAP trial?**
  - a. Inflation to 45 cm H<sub>2</sub>O positive end-expiratory pressure (PEEP) from baseline for five minutes
  - b. Inflation to 65 cm H<sub>2</sub>O PEEP from baseline for five minutes
  - c. Stepwise inflation from baseline to 40 cm H<sub>2</sub>O PEEP in 5 cm H<sub>2</sub>O increments every five minutes
  - d. Stepwise inflation from baseline to 40 cm H<sub>2</sub>O PEEP in 10 cm H<sub>2</sub>O increments every two minutes
4. **Which one of the following culture results was used to diagnose ventilator-associated pneumonia in the ANTHARTIC trial?**
  - a. Any positive bacterial culture (blood/sputum/urine)
  - b. Any positive lower respiratory tract culture
  - c. 10<sup>6</sup> colony forming units (CFU) for bronchoalveolar lavage (BAL)
  - d. 10<sup>6</sup> CFU for endotracheal aspirates

#### CME/CE OBJECTIVES

Upon completion of this educational activity, participants should be able to:

- identify relevant topics in the practice of critical care medicine;
- utilize recommendations from current clinical guidelines; and
- manage common critically ill patient and ICU administration scenarios.

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