Inflammation and the Host Reponse to Injury, a Large-Scale Collaborative Project: Patient-Oriented Research Core—Standard Operating Procedures for Clinical Care

II. Guidelines for Prevention, Diagnosis and Treatment of Ventilator-Associated Pneumonia (VAP) in the Trauma Patient

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Ventilator-associated pneumonia (VAP*) is the most common nosocomial infection encountered in the ICU setting. Injured patients are particularly prone to VAP due in part to injuries such as direct chest trauma with pulmonary contusion and inability to control oropharyngeal secretions associated with traumatic brain injury. Post-injury immunosuppression is a recognized complicating factor of severe injury. Furthermore, common therapies used in caring for injured patients, such as blood transfusion, total parenteral nutrition and repeated trips to the operating room add to this immunocompromised state. The Centers for Disease Control (CDC), through the National Nosocomial Infections Surveillance System (NNIS), report that the median rate of VAP per 1000 ventilator days for patients in trauma ICU's (11.4) was higher than any other individual type of surgical ICU (general surgery, cardiac surgery, neurosurgical, etc.). This rate was more than double that seen in medical (3.7) or coronary care (4.0) ICU's.[1]

The mortality and morbidity attributable to VAP is difficult to ascertain. In a matched cohort study looking at a mixed population, the relative risk of death attributable to pneumonia was 32%.[2] This increase was only significant in medical ICU patients where the relative risk of death attributable to pneumonia was 65%, suggesting an episode of VAP tips the balance for the medically frail. It is likely that surgical patients, by virtue of either being selected by surviving operative intervention (or their injuries) have adequate reserve such that an episode of VAP is less likely to be fatal. However, the additional length of stay (4–6 days) and associated costs,[3] coupled with the detrimental effects of antimicrobial use on ICU ecology, calls for aggressive prevention strategies and a practical, evidence-based approach to managing VAP in critically ill trauma patients.

Despite its common occurrence, there is still no agreed upon "gold standard" for the diagnosis of VAP and contro-

versy persists regarding its true incidence. Generalized guidelines for the prevention and management of VAP have recently been forwarded by the Canadian Critical Care Society[4] as well as the American Thoracic Society and Infectious Disease Society of America.[5] However, the strategy used to take general guidelines and make them operational for a homogenous patient population such as trauma has not been done. In the injured population specific guidelines are especially needed for the diagnosis of VAP where pulmonary contusion may confound chest radiograph interpretation and fever, tachycardia and leukocytosis may be secondary to the systemic inflammatory response (SIRS) induced by the injury. Strict definitions for the diagnosis of VAP along with appropriate antibiotic treatment guidelines may result in fewer patients without VAP being treated and reduce antimicrobial resistance.

As part of the Inflammation and the Host Response to Injury Large-Scale Collaborative Research Program, the participating investigators took existing evidence-based data and guidelines for prevention, diagnosis and treatment of VAP and developed a standard operating procedure (SOP) to manage these patients. These procedures do not address prevention strategies related to ventilator maintenance (circuit changes, humidifiers, suction devices, etc.), but are focused on prevention strategies targeting direct clinical patient care. The primary purpose of this SOP was to standardize the manner in which trauma patients are managed in relation to prevention, diagnosis and treatment of VAP across the centers enrolling patients into the Program's clinical trials. No attempt was made to re-classify and grade all available evidence, rather the goal was to develop a uniform approach to injured patients from evidence based guidelines and data already in print.

Protocol Goals

● Reduce the incidence of VAP in ventilated trauma patients using standardized prevention strategies.
● Define the necessary clinical criteria for the diagnosis of VAP in patients with suspected VAP.
● Provide clinical guidelines for the treatment of VAP that ensures antimicrobial therapy is initiated and discontinued appropriately.

Protocol Rationale

Prevention of Ventilator-Associated Pneumonia (VAP)

Most episodes of VAP occur as a result of aspiration of contaminated oropharyngeal and to a lesser extent gastric secretions around the endotracheal tube. While hematogenous spread from a distant site can occur, it is considered rare in comparison to direct micro- or macro-aspiration. Thus, prevention of VAP can be most effectively accomplished with a number of strategies directed at either decreasing the microbiologic load of the aspirate, and/or minimizing the volume of aspirate.

The greatest risk factor for the development of VAP is the duration of mechanical ventilation. The longer patients are intubated with an endotracheal tube, the greater the risk for the development of VAP. Thus, an important and sometimes overlooked prevention strategy is implementing a ventilator management strategy that ensures liberation from the ventilator at the earliest time. To this aim, the Inflammation and the Host Response to Injury Large-Scale Collaborative Research Program has previously published their Ventilator Management Guideline in this Journal.[6]

Institution of an ICU oral hygiene program has been shown to be effective in decreasing the incidence of VAP. There is Level II evidence showing that use of the antiseptic agent chlorhexidine gluconate, as part of an oral hygiene program of frequent tooth-brushing, and deep suctioning of oral and pharyngeal/subglottic secretions, is associated with a reduction in the incidence of VAP in trauma patients.[7]

Techniques that minimize the volume of aspirate have also been shown to be effective in decreasing VAP rates. In patients whose injuries do not specify the need for supine positioning, elevation of the head of the bed greater than 30° from horizontal has been shown to be an effective VAP prevention measure. In those that must remain supine, reverse Trendelenberg positioning can be effective. Level I evidence from a randomized controlled trial, has shown the relative risk reduction of this relatively simple intervention was almost 80%,[8] with the principal VAP risk factors in this study being supine positioning and enteral feeding. As a corollary, prevention of gastric distention and vomiting or gross reflux with naso- or oro-gastric tube should be routine. These tubes should be removed at the earliest clinically appropriate time to maintain the integrity of the lower esophageal sphincter. Additionally, sucralfate or H2-blockers should be used for stress gastritis prophylaxis as they are equally effective in preventing stress-induced bleeding. Antacids should be avoided since the volume and dwell time required to effectively mitigate bleeding poses an increased risk for aspiration. Early surgical feeding access either at the time of initial abdominal surgery or with percutaneous techniques in those with prolonged need for intubation (e.g. traumatic brain injury) should also be considered.

Minimizing transfer of contaminating organisms from the health-care worker to patient decreases a number of nosocomial infections including VAP. Transmission of microorganisms from health-care workers hands to patients and devices, including ventilator circuits and endotracheal tubes, is well documented. There is Level I evidence to show hand-washing, including frequent use of alcohol-based antiseptic preparations as well as frequent health-care worker glove change, is associated with a reduction in nosocomial infections.[9]

Recent studies from ICUs that have instituted a number of the above described VAP prevention strategies together as a "VAP prevention bundle" have been highly successful with reductions in VAP rates that approach 50%.[10] Further, out-

Table 1 Clinical Pulmonary Infection Score

	Points
Temperature (°C)	
≥ 36.5 and ≤ 38.4	0
≥ 38.5 and ≤ 38.9	1
≥ 39 or ≤ 36.5	2
Blood leukocytes, mm^3	
$\geq 4,000$ and $\leq 11,000$	0
$\leq 4,000$ or $\geq 11,000$	1
$\leq 4,000$ or $\geq 11,000$ and band forms $\geq 50\%$	2
Tracheal secretions	
None or scant	0
Presence of non-purulent secretions	1
Presence of purulent secretions	2
Oxygenation: PaO_2/FiO_2	
≥ 240, ARDS or Pulmonary contusion	0
≤ 240 and no ARDS	2
(ARDS defined as $Pa_{O2}/Fi_{O2} \leq 200$, PAWP ≤ 18 mm Hg and acute bilateral infiltrates)	
Pulmonary radiography	
No infiltrate	0
Diffuse (or patchy) infiltrate	1
Localized infiltrate	2

Adapted from Singh, N et al.[11]

side regulatory agencies are starting to require VAP prevention strategies and will be auditing compliance in the future. Standard operating procedures are presented that reflect the above recommendations based on Level I and II evidence.

Standard Operating Procedure for the Diagnosis of VAP

The diagnosis of VAP has been made on the basis of a constellation of signs and symptoms, including fever, leukocytosis, abnormal findings on chest x-ray and production of purulent respiratory secretions, which when cultured, reveal pathogenic organisms on Gram's stain and microbiologic culture results. Unfortunately, there is no consensus on which combination of findings yields an accurate diagnosis of VAP. This poses difficulty in the injured patient where pulmonary contusions and aggressive resuscitation along with a concomitant reperfusion injury can result in an abnormal chest radiograph and the systemic inflammatory response syndrome (SIRS), common in severely injured patients, can mimic infection.

The clinical pulmonary infection score (CPIS, see Table 1) has been developed to estimate the likelihood that a patient has nosocomial pneumonia. In a group of hospitalized medical patients, those with a score of ≤ 6 had a low probability of having pneumonia when compared with those with a score of > 6.[11] Further, when the CPIS was used to guide antimicrobial therapy, there was less antimicrobial use and a reduction in the risk of infections due to resistant organisms. Unfortunately, using the CPIS > 6 threshold by itself for a

diagnosis of VAP is neither sensitive nor specific. In a retrospective review of prospectively collected data, CPIS was compared with quantitative broncho-alveolar lavage (BAL) cultures to evaluate the operating characteristics of CPIS > 6 in the diagnosis of VAP. Of 113 patients who did not have VAP (quantitatively negative BAL cultures), 53 had a CPIS ≤ 6, and 60 had a CPIS > 6. Of the 88 patients that had VAP diagnosed by quantitatively positive BAL cultures, 10 had CPIS ≤ 6, and 78 had a CPIS > 6. This resulted in a sensitivity, specificity, positive predictive value and negative predictive value of 89%, 47%, 57% and 84% respectively.[12] Thus, based on Level II evidence, this SOP does NOT use CPIS independently to diagnose VAP. However, CPIS is used as an initial screening tool to identify patients who may be at a higher likelihood of having a diagnosis of VAP, acknowledging that the variable presentation of VAP seen in trauma patients may lead to a variety of clinical parameters that heighten suspicion for a diagnosis of VAP. Thus, the purpose of including CPIS in the SOP was to standardize and quantify the factors that increase clinical suspicion for VAP across the participating centers and assure that patients would have quantitative cultures obtained for similar clinical criteria.

In patients who have elevated CPIS scores, VAP diagnosis is only confirmed after results of respiratory cultures are known. Routine sputum specimens collected from an endotracheal tube are notoriously non-specific in the diagnosis of VAP as the endotracheal tube and trachea quickly become colonized shortly after intubation. Most recent data that evaluate the criteria for treatment with antibiotics in a presumed diagnosis of VAP have utilized semi-quantitative or quantitative protected sampling of the lower respiratory tract. Semi-quantitative and quantitative cultures, while not 100% sensitive and specific, can help distinguish between colonization and infection.[13] Croce and colleagues were the first to show the importance of using quantitative cultures in injured patients to distinguish VAP from those with non-infectious systemic inflammatory response syndrome.[14]

There are a number of techniques that can be utilized to obtain respiratory samples for quantitative culture evaluation. These include bronco-alveolar lavage (BAL) obtained bronchoscopically, BAL obtained non-bronchoscopically using protected or telescoping catheters, and protected specimen brush (PSB). However, there is no gold standard, even when compared with autopsy,[15] but a therapeutic strategy with BAL as the cornerstone of diagnosis, has been shown to reduce mortality.[16] In a recent randomized, controlled multicenter study, management strategies based on an invasive quantitative diagnosis (BAL or PSB) were associated with improved 14-day survival, earlier improvement from organ dysfunction and decreased antibiotic complications compared with a strategy based on clinical criteria and routine endotracheal sputum culture without protected lower respiratory tract sampling.[16] Based on Level I evidence, we present standard operating procedures for the diagnostic approach to VAP.

Standard Operating Procedures for the Treatment of VAP

Treatment of suspected VAP should begin early with empiric therapy based on the local antibiogram aimed at the common pathogenic organisms in each specific ICU. Studies have shown if the initial antibiotic therapy is inadequate to cover pathogenic organisms that are ultimately isolated on subsequent culture then mortality is significantly increased. Further, if antibiotic selection is either initially withheld or subsequently escalated once the results of cultures are known, mortality is greater than if the correct antibiotic selection was made empirically.[17] The most common organisms isolated from respiratory cultures of patients suspected of VAP are *S. aureus* and *P. aeruginosa*. The most recent CDC surveillance data suggests that methicillin-resistant *S. aureus* accounts for nearly 60% of all *S. aureus* isolates in the ICU. Likewise, resistant *P. aeruginosa* is a growing ICU problem with carbapenem, quinolone and 3rd-generation cephalosporin resistance measured at 21%, 30% and 32% respectively.[1] Empiric antimicrobial coverage should account for the resistance patterns of common pathogenic isolates in any particular unit. Once microbiologic results including sensitivities are known, "de-escalation" of antimicrobial coverage to fit the culture results is indicated, using the most narrowly focused antibiotics appropriate. The concept of stopping antibiotics if quantitative cultures are less than threshold values is supported in the literature.[16] It has also been shown that unnecessary use of antibiotics for VAP increases the likelihood of superinfection with multi-resistant organisms.[2]

The duration of antibiotic treatment for a confirmed case of VAP has received considerable attention in the literature. Recent data suggests that antibiotics can be stopped once clinical signs of infection have resolved. This may also decrease the incidence of secondary pneumonias with multi-resistant organisms.[18,19] A recent study showed that an antibiotic discontinuation policy based on a pre-defined clinical response to antimicrobial therapy was associated with a shorter duration of antibiotic use and no difference in the occurrence of secondary VAP episodes when compared with conventional antibiotic management. Generally, antibiotic duration was on average 2 days less in the group that followed the antibiotic discontinuation policy and totaled approximately six days.[19] There is some biological rationale for shorter courses of antibiotics for VAP. One study followed daily cultures and clinical signs for 2 weeks after diagnosis of VAP. These authors showed that most clinical signs had resolved by day 6 of therapy and that in the case of *H. influenzae* and *S. pneumoniae* all organisms were eradicated. Enterobacteriaceae, *S. aureus,* and *P. aeruginosa* persisted despite in vitro sensitivity and suggests that the airway will remain colonized with these organisms no matter how long the course of antibiotics.[20] In a multi-center randomized trial there were no differences in mortality or recurrent infection between patients with quantitative culture positive VAP who were treated for 8 days of antibiotics versus those treated for 15 days. Those treated 15 days had greater antibiotic use and greater emergence of multi-resistant organisms, while the subset of patients who grew non-lactose fermenting organisms such as *P. aeruginosa* and *A. Baumanii* had more recurrent infections when treated for 8 days.[21] Based on Level I and II evidence presented, standard operating procedures for the treatment of VAP is presented.

Protocol Summary

A. All ICUs should have a defined VAP prevention program. This program should include education of all personnel with direct patient or ventilator contact. Ongoing compliance assessment and feedback should be made available to patient caretakers with the goal of improving prevention compliance.

B. Patients with suspected pneumonia within 72 hours of admission and intubation should have their diagnosis based on a constellation of signs and symptoms that are determined locally for community acquired pneumonia and do not need their diagnosis confirmed by invasive quantitative culture analysis. A high quality sputum sample with minimal epithelial cells, large numbers of leukocytes and large growth of one predominant organism should be considered.

C. Patients should have a daily assessment of their clinical pulmonary infection score to determine who should undergo invasive quantitative culture analysis. Once a CPIS threshold has been attained, quantitative cultures should be obtained by bronchoscopic sampling. Alternatively, non-bronchoscopic ("blind") techniques may be utilized to obtain samples. Data from Wood and colleagues obtained in injured patients suggests that bronchoscopic and blind techniques used for obtaining deep respiratory samples for culture have equivalent sensitivity and specificity.[22] Standardized techniques should be utilized for obtaining and processing quantitative samples. Controversy exists regarding the quantitative threshold that is required to make a diagnosis of VAP. In the trauma population, independent data from Croce[23] and from Miller[24] support a diagnostic threshold $\geq$ 100,000 colony forming units(CFU)/mL of lavage fluid. The CDC criteria support a diagnostic threshold $\geq$ 10,000 CFU/mL. Utilizing the higher threshold will result in more false negative diagnosis; a rate that both Croce and Miller suggest is approximately 15% of cases. Alternatively the lower threshold potentially results in over-treating patients who do not have VAP. In the absence of definitive evidence to support any threshold, the members of this Large Scale Collaborative Program chose to use a threshold $\geq$ 10,000 CFU/mL to minimize the risk of not treating a patient with VAP. Suspicion of VAP should prompt rapid procurement (i.e. less than 4 – 6 hours) of lower respiratory tract invasive specimens for quantitative culture, before institution of antimicrobial therapy, but should not delay

therapy in critically ill patients.

D. Broad spectrum empiric antibiotics should be started as soon as the sample for quantitative analysis has been obtained. Antibiotic choice should be based on unit-specific antibiograms. A regimen should be chosen that will cover the pathogenic organisms most likely to be retrieved from pulmonary cultures.

E. Antimicrobial therapy should be discontinued if quantitative cultures do not meet or exceed the threshold level of growth.

F. If the growth of quantitative cultures exceeds the threshold for the technique employed then antibiotics should be continued and adjusted or "de-escalated" based on culture and sensitivity results. Antibiotics should be stopped once resolution of clinical signs for greater than 24 hours has occurred. In the absence of symptom resolution, antibiotics should be stopped after 7–8 days of therapy.[5] Patients should be reassessed for signs of infection recurrence, particularly if the initial culture returned non-lactose fermenting gram-negative rods.

Protocol Details

Strategies to Prevent Ventilator-Associated Pneumonia

1. Standardized ventilator weaning protocol. This protocol should include daily evaluation for readiness to undergo a spontaneous breathing trial. Spontaneous breathing trials should be performed when indicated. Patients should be liberated from the ventilator shortly after passing their spontaneous breathing trial. The protocol used by this Large Scale Collaborative Project has been previously described.[6]

2. Oral hygiene program for all intubated patients. This program should include hygiene at least once every eight-hour shift. This program should include tooth brushing, tongue and gum brushing, and irrigation and suctioning of the oropharynx. The use of a chlorhexidene rinse (0.12%) at least twice daily is recommended.

3. Program to minimize aspiration of microbiologically contaminated secretions.

a. Elevate the patient's head of bed greater than 30° above horizontal. In patients who must be kept flat secondary to spinal fractures, use reverse Trendelenberg positioning to attain head of bed elevation.

b. Use deep suctioning to clear pooled secretions in the oropharynx that collect above the endotracheal tube balloon. This suction tip should be changed every shift and kept clean (but not sterile).

c. Avoid gastric distention. Follow gastric residuals by the use of an oro- or nasogastric tube and adjust enteral feeding attempts appropriately. Consider early surgical or percutaneous routes for nutritional access.

d. Clear ventilator tube condensation to avoid back wash into the endotracheal tube.

e. Avoid antacids to control gastric pH due to the volume required for efficacy. Utilize sulcralfate or H2-blockers

until enterally fed. Proton pump inhibitors should be used for the treatment of clinically evident upper gastrointestinal bleeding.

4. Institute a program that encourages frequent hand washing and glove use when direct patient care is required. Have antiseptic solutions at every bedside for ease of healthcare worker compliance.

5. Develop an education, compliance monitoring and feedback program within the ICU to encourage and monitor program success.

Diagnosis of Ventilator-Associated Pneumonia

An algorithm for the diagnosis and treatment of VAP is presented in Figure 1.

1. The clinical pulmonary infection score (CPIS; Table 1) should be determined daily and when concern for any infection arises.

a. A CPIS > 6 identifies a patient that is more likely to have VAP.

b. Those with a CPIS ≤ 6 should have a clinical assessment performed looking for other sites of infection.

c. If the suspicion for VAP is low, no further work up is necessary, save for an evaluation of other potential sources of infection.

d. If, after the evaluation of a patient with a CPIS ≤ 6, the suspicion for VAP is high, then patients will be evaluated as if their CPIS > 6.

e. All patients with CPIS > 6 should undergo invasive diagnostic techniques to obtain lower respiratory tract samples for quantitative culture.

2. Quantitative invasive techniques should be utilized to obtain deep respiratory samples.

a. The bronchoscope can be used to obtain samples from suspicious areas based on chest radiograph or other physical findings. Either protected specimen brushing or broncho-alveolar lavage (BAL) may be utilized. If BAL is utilized, five separate 20 mL aliquots of non-bacteriostatic normal saline should be individually used to lavage and collect samples from the lower respiratory tract. All five collections should be pooled and sent for quantitative culture, identification, sensitivity and Gram's stain.

b. Alternatively samples for quantitative cultures may be obtained by "blind BAL" techniques. A number of commercial catheters are available that can be guided to either the left or right mainstem bronchus (BAL-CATH; Kimberly-Clark, Draper, UT), as determined by suspicion on chest radiograph. These catheters use either telescoping or protected tips to minimize contamination while traversing the endotracheal tube and trachea. Five 20 cc aliquots should be instilled, retrieved and processed as described above.

c. CDC criteria for positive quantitative culture results are used to confirm the diagnosis of VAP. The following CDC defined threshold values will confirm a diagnosis
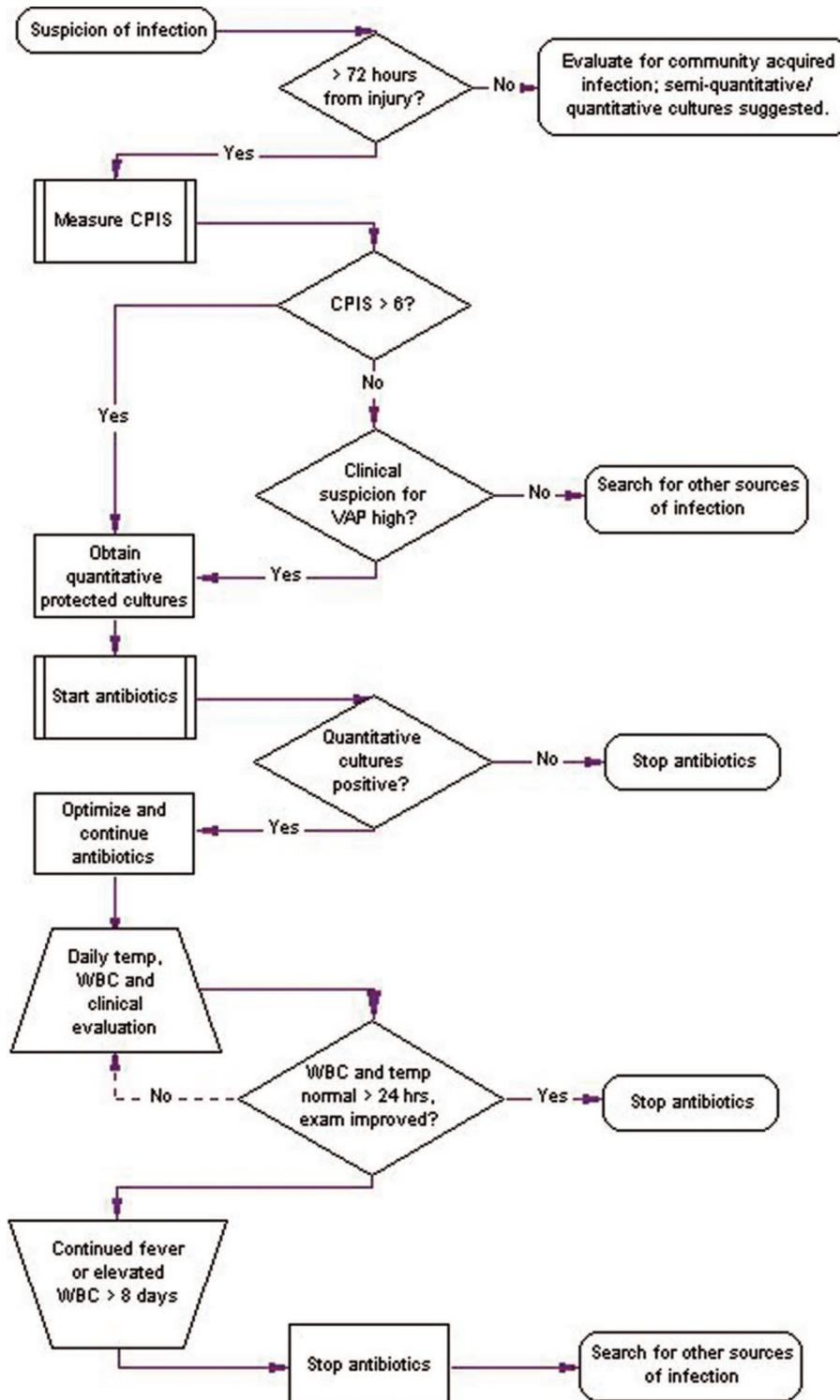
Fig. 1. *Algorithm for the Diagnosis and Treatment of VAP*

of VAP and have been generally accepted in the literature. [http://www.cdc.gov/ncidod/hip/NNIS/NosInfDefinitions.pdf]

i. Bronchoscopic or non-bronchoscopic (blind) BAL: $> 10^4$ colony forming units/mL

ii. Bronchoscopic protected specimen brush: $> 10^3$ colony forming units/mL

Those patients with quantitative cultures that do not meet CDC threshold will not be given a diagnosis of VAP.

Treatment of VAP

1. The treatment of VAP should depend on the unit-specific local antibiogram. Empiric treatment directed against likely pathogens should be instituted as soon as possible after cultures are obtained.

2. Empiric antibiotic treatment should be directed at the common sensitivities of pathogenic organisms typically found in the respiratory cultures from the ICU. Inclusion of gram-positive coverage with activity against MRSA and broad-spectrum combination therapy for *P. aeruginosa* should be considered.

3. Once culture results and sensitivities are known therapy should be tailored to the narrowest possible antibiotic selection possible (de-escalation). If, after 48 -72 hours, quantitative cultures do not meet CDC threshold for VAP, then antibiotics should be stopped.

4. The duration of antibiotic treatment should be based on the patient's clinical response.[5] Antibiotics should be continued until the patient has had an appropriate clinical response, is afebrile with a normal leukocyte count, and has diminished sputum production and improving respiratory status for at least 24 hours. Predetermined lengths of treatment for 10, 14 or 21 days should not be followed. In most cases, an appropriate clinical response will be noted and antibiotics can be stopped in 6 – 8 days. Consideration for longer antibiotic courses may be entertained if the patient remains either febrile or has a continued leukocytosis, particularly when non-lactose fermenting organisms are cultured.

Summary

Ventilator-associated pneumonia remains a common, difficult clinical problem in the trauma ICU. This paper describes the current procedures used by the clinical centers participating in The Inflammation and Host Response to Injury Large Scale Collaborative Program. It is evidence based where good evidence exists and relies on expert opinion where there is a void. The goal of this SOP was to standardize the management of injured patients across multiple study sites. The value of SOP adherence is to minimize variability in clinical care and study outcomes on large numbers of similar patients. It should be appreciated that this SOP is dynamic and will undergo change as new data are identified.

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EDITORIAL COMMENT

Hospital acquired pneumonia, specifically ventilator-associated pneumonia (VAP), remains a major cause of morbidity and mortality in our trauma patients. The association between VAP and death is strong in critically ill patients, but it is thought that these patients are the "medically frail," and that surgical and trauma patients have adequate reserve so that an episode of VAP is less likely to be fatal.[1] It has been suggested that VAP may be a marker of injury severity and not necessarily associated with mortality except, perhaps, in the most severely injured. However, Magnotti[2] demonstrated that VAP was independently associated with death in the less severely injured patients (ISS < 25). This association was not present in the more severely injured, since the effect of injury on outcome was more pronounced. Unfortunately, much of the research regarding VAP has been performed by non-surgeons on non-surgical patients, making extrapolation to the trauma patient difficult at best.

The National Institutes of Health has recognized the unique issues of the trauma patient and has committed to increase our understanding of inflammation and the host response to injury. To that end, the Inflammation and the Host Response to Injury Large Scale Collaborative Research Program Investigators have outlined their Standard Operating Procedures for the prevention, diagnosis, and treatment of VAP in the trauma patient.[1] These investigators, along with the NIH, are emphasizing the significance of VAP in the trauma patient. The concepts presented for VAP prevention in this paper are sound. The diagnosis of VAP will be made using quantitative cultures. While one may quibble regarding the diagnostic threshold, the important point is that there will be more widespread use of quantitative cultures. Unfortunately, the investigators will be using the Clinical Pulmonary Infection Score (CPIS) to screen patients for VAP. While the CPIS may be beneficial in non-trauma patients, it is not a helpful screening tool for trauma patients. The CPIS measures the pulmonary inflammatory response, which is separate and distinct from pulmonary infection. There is little correlation between *inflammation* and *infection* in this patient population.[3] Perhaps the investigators will consider either less reliance on CPIS as a screening tool, or lower the CPIS threshold as a trigger for quantitative cultures.

The operating procedures presented by these investigators are an important step for care of our injured patients. Recognizing the difference between inflammation and infection is critical, since antibiotic therapy is not beneficial for inflammation. This collaborative research project is quite promising, and we all anxiously await the results.

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