Current Infectious Disease Reports (2019) 21: 50
https://doi.org/10.1007/s11908-019-0708-3

HEALTHCARE ASSOCIATED INFECTIONS (G BEARMAN AND D MORGAN, SECTION EDITORS)

Ventilator-Associated Pneumonia: Diagnostic Test Stewardship and Relevance of Culturing Practices

Blaine Kenaa[1] · Mary Elizabeth Richert[2] · Kimberly C. Claeys[3] · Andrea Shipper[4] · Kaede V. Sullivan[5] · Gregory M. Schrank[6] · Lyndsay M. O'Hara[7] · Daniel J. Morgan[7] · Carl Shanholtz[1] · Surbhi Leekha[7]

Published online: 21 November 2019

Abstract

Purpose of Review Ventilator-associated pneumonia (VAP) is one of the most common infections in the ICU. Prompt diagnosis is vital as mortality increases with delayed antibiotic therapy. However, accurate diagnosis is challenging due to non-specific clinical features in a complicated patient cohort. Microbiological culture data remains a crucial aspect in confirming diagnosis.
Recent Findings Literature data comparing the benefit of invasive respiratory sampling to non-invasive is inconclusive. Differences in culturing practices translate in overidentification of organisms of unclear significance. Positive culture data in a low pre-test probability does not differentiate between true infection and colonization resulting in overtreatment. Furthermore, there are also opportunities for modifying the reporting of respiratory tract cultures that can better guide antimicrobial therapy.
Summary Under the umbrella of antimicrobial stewardship, diagnostic stewardship can be incorporated to create a systematic approach that would target culturing practices to match the right pre-test probability. Ideal outcome will be targeting cultures to the right patient population and minimizing unnecessary treatment.

Keywords Ventilator-associated pneumonia · Diagnostic stewardship · Antimicrobial stewardship · Selective culture reporting · Invasive respiratory culturing · Endotracheal aspirate

Introduction

Ventilator-associated pneumonia (VAP) is one of the most common infections in the intensive care unit (ICU) with an incidence that ranges from 10 to 40% [1, 2]. A diagnosis of VAP significantly increases mortality and as such requires prompt intervention [1, 2]. Estimates of temporal changes in VAP incidence are inconsistent between sources show inconsistency between estimates from the (MPSMS) and (NHSN). VAP incidence from the Medicare Patient Safety Monitoring

This part is part of Topical Collection on *Healthcare Associated Infections*

✉ Blaine Kenaa
Blaine.kenaa@som.umaryland.edu

Mary Elizabeth Richert
Mary.richert@som.umaryland.edu

Kimberly C. Claeys
kclaeys@rx.umaryland.edu

Andrea Shipper
ashipper@hshsl.umaryland.edu

Kaede V. Sullivan
kaede.ota@tuhs.temple.edu

Gregory M. Schrank
gschrank@som.umaryland.edu

Lyndsay M. O'Hara
lohara@som.umaryland.edu

Daniel J. Morgan
dmorgan@som.umaryland.edu

Carl Shanholtz
Cshanholt@som.umaryland.edu

Surbhi Leekha
sleekha@som.umaryland.edu

Extended author information available on the last page of the article

System based on randomly selected samples from the Centers for Medicare & Medicaid Services of in-hospital adverse events suggests a decline in incidence from 2005 to 2011 [3]. In contrast, VAP incidence based on National Healthcare Safety Network surveillance data from acute care hospitals shows no significant change over a similar time period [4, 5] [3]. While this is likely due to differences in definitions, it reflects challenges related to the diagnosis and clinical definition of VAP.

Currently, there is wide variation in the diagnostic criteria used by clinicians for VAP and the methods used for respiratory tract sampling [6]. Clinical uncertainty of true VAP and routine availability of cultures obtained using non-invasive methods facilitate high-intensity culturing practices. Frequent and easy identification of bacteria colonizing the respiratory tract contributes to VAP overdiagnosis, which, in turn, leads to antibiotic overuse in the ICU [7••, 8]. Variations in laboratory-reporting practices of respiratory tract culture results (e.g., bronchoalveolar lavage (BAL) vs endotracheal aspirate (ETA)) can also cause confusion among clinicians during interpretation, influencing the decision-making process around antibiotic therapy [6]. Diagnostic stewardship aims to systematically improve the use of diagnostic testing in each of the phases of ordering, specimen collection, and reporting [7••]. While there is evidence that improving culturing practices related to the diagnosis of urinary tract and *Clostridioides difficile* infections can reduce testing and subsequent antibiotic use, this concept is relatively novel in the case of respiratory culturing especially in patients on mechanical ventilation who are at a high risk for VAP [7••, 9, 10].

Diagnostic stewardship strives to evaluate the validity of ordering and proceeding with culturing in the setting of low pre-test probability and ensures optimal specimen collection technique and transport to the laboratory, and interpretation of reported cultures. Ultimately, like its partner antimicrobial stewardship, diagnostic stewardship aims to ensure appropriate delivery of antibiotics to the right patient for diagnosis of true infection [7••]. In this paper, we first review various points in the VAP diagnosis pathway that highlight the need and opportunities for diagnostic stewardship, and then offer potential solutions.

Search Methods

A medical librarian conducted structured searches based on relevant key words that included terms for mechanical ventilation, pneumonia, and diagnosis or diagnostic and antimicrobial stewardship. Electronic databases included PubMed, Embase (embase.com), and the Cochrane Central Register of Controlled Trials (Wiley). Search strategies included both text words and subject headings, and searches were customized to each database. The search results were limited to include only studies with adult subjects and those published since 2014. An additional search was conducted on PubMed and Embase (2012–present) with search terms including invasive versus non-invasive culturing, microbiology reporting, culture reporting, and antibiotic stewardship.

Search Results

Initial searches were completed on September 13, 2018, and yielded 1642 unique citations. Two reviewers screened those citations by reviewing titles and abstracts for relevant articles, resulting in a total of 38 publications that were reviewed in full and summarized below under [1] need for VAP diagnostic stewardship and [2] potential implementation opportunities in the pre-analytic, analytic, and post analytic phases of diagnostic stewardship for VAP.

Need for Diagnostic Stewardship in VAP Diagnosis

Minimizing unnecessary antibiotic use and selective pressure is crucial in the ICU where patients are given numerous courses of antibiotic therapy [6]. Although culture results can be helpful for antimicrobial de-escalation in the appropriate clinical scenario, when cultures are positive in the absence of underlying pneumonia, they can lead to unnecessary antimicrobial use and selection for multi-drug resistant (MDR) bacteria [11]. Antimicrobial stewardship (AMS) has been instrumental in helping guide health care providers with appropriate antibiotic selection, limiting the adverse consequence of unnecessary antibiotic exposure, and improving antibiotic-related patient outcomes [12]. However, there has been a growing realization that inappropriate testing for infection can lead to positive cultures that reflect colonizing flora as opposed to agents of true infection, pointing to a need for *diagnostic* stewardship as an important adjunct to antimicrobial stewardship [7••]. In 2014, Nussenblatt et al. devised a retrospective study to evaluate the state of VAP diagnostic framework and identify gaps in the decision-making process over a 1-year period in their medical, surgical, and subspecialty surgical ICUs. A multidisciplinary team of clinicians and pharmacists reviewed 231 clinically diagnosed cases of VAP. Two independent reviewers used clinical, microbiological, and radiographic data to adjudicate the diagnosis of VAP and found that 68% of the cases did not have VAP on day 3 of their clinical diagnosis. In addition, respiratory culturing on day 3 was associated with prolonged antibiotic treatment (39% vs 16%, $p < 0.01$) [8]. Furthermore, 50% of the cultures in this study were reported positive for polymicrobial growth of common respiratory flora of unclear significance. This highlights the challenge that clinicians face when determining

microbiological growth as a contaminant, colonization, or normal flora when managing an ICU patient.

Pre-analytic Issues: Ordering

Identification of VAP Based on Clinical Features

Clinical features of VAP are non-specific. Suspicion for VAP often begins when mechanically ventilated patients develop worsening gas exchange, fever, or radiographic evidence of chest infiltrates. Similarly, changes in quality or quantity of respiratory secretions can raise suspicion of VAP even in the absence of radiologic or ventilatory changes. However, these clinical findings are all non-specific for pneumonia [13]. In the presence of cardiac and pulmonary co-morbidities, radiographic imaging has been shown to have poor diagnostic accuracy as pulmonary edema, atelectasis, and aspiration pneumonitis and mucus plugging can have similar appearances [14] [15]. Previously, the Clinical Pulmonary Infection Score (CPIS) was employed to risk stratify and initiate antibiotics on patients with suspected VAP. However, a prospective study of 508 patients by Quick et al. showed that CPIS has insufficient diagnostic accuracy with a 61% sensitivity and 78% specificity [13]. This was consistent with a previous large meta-analysis that showed a sensitivity of 65% and specificity of 64% [16]. Currently, the American Thoracic Society (ATS) no longer recommends use of CPIS for diagnosis of VAP [4]. Overall, the lack of definitive clinical criteria highlights the limitation of relying on clinical features as a diagnostic tool. This leads to a heavy reliance on culture results to help with VAP diagnosis, compounding the potential for overdiagnosis in the setting of positive culture results coupled with low pre-test clinical probability of VAP.

Invasive Versus Non-invasive Respiratory Tract Sampling

Specimen acquisition approaches can be invasive or non-invasive and there are relative merits and drawbacks to both (Table 1). Current standard of care in the diagnosis of VAP includes the isolation of lower respiratory microbes, both to confirm the diagnosis and guide antimicrobial therapy. However, approaches to isolate the lower respiratory culture vary by clinician and institutional practice [6]. The practice of invasive sampling includes bronchoscopy with bronchoalveolar lavage (BAL), bronchial washing, and mini-BAL that is usually performed by the respiratory therapist. Mini-BAL does not require bronchoscopy; a sterile catheter is advanced 3–5 cm beyond the endotracheal tube (ETT) and advanced to the distal portion of the lung with instillation of sterile saline and aspiration of contents. Isolated respiratory samples are further analyzed quantitatively. Non-invasive sampling of the respiratory tract includes endotracheal aspiration (ETA) where samples are collected from the ETT and sent for qualitative, quantitative, or semi-quantitative analysis.

In 2014, Berton et al. published a meta-analysis of five trials that included a total of 1240 patients. Three studies compared invasive sampling with quantitative culturing to non-invasive sampling with qualitative culturing [17–19]. Two of the studies compared invasive to non-invasive sampling with quantitative culturing [20, 21]. The primary outcome was 28-day mortality and the secondary outcomes were change in antibiotics, number of days on mechanical ventilation, and ICU length of stay. Overall, there was no difference in 28-day mortality in any of the primary or secondary outcomes [4, 22].

The goal of invasive sampling, i.e., BAL, is to perform direct sampling of actual part of the lung that is involved by infection, reduce the recovery of colonizing bacteria and oral contaminants, and minimize the risk of missing the true pathogenic organism. While current practice of BAL is based on studies that suggest that the actual part of the lung sampled does not matter as long as sampling is from the lower airway, differences in bacterial recovery from right and left lung were demonstrated in a recent study by Bello et al. The investigators quantitatively analyzed right and left lung samples in 79 patients with the primary goal of evaluating microbiological concordance and potential impact on antibiotic selection. In 40% of cases, there was discordance between BAL cultures from the left and the right lung [14]. While this discordance did not affect appropriate antibiotic selection because of the frequent use of broad-spectrum antibiotics, opportunity to provide potentially narrow antimicrobial therapy, directed at the true pathogenic organism based on site of infection, was identified.

Table 1 Comparison of non-invasive and invasive sampling of the lower respiratory tract

	Non-invasive sampling	Invasive sampling
Pros	• Less costly • Ease of sampling • Decreased risk of adverse events • Recommended by 2016 ATS/IDSA guidelines	• Less susceptibility for contamination • Faster cessation of antibiotics • Recommended by ERS 2017 guidelines
Cons	• Increased risk of contamination • Longer antibiotic courses • Higher risk of false positives	• Dependent on advanced provider training and availability • Increased cost and resources • Increased risk of adverse events

Aspiration, both overt and micro-aspiration, is a common reason for respiratory compromise in ventilated ICU patients. Clinically differentiating chemical pneumonitis from bacterial aspiration pneumonia is challenging. The presence of radiographic infiltrate with systemic signs of infection and purulent tracheobronchial aspirate can be seen in both, with similar outcomes in prolonging mechanical ventilation and ICU length of stay [23••]. A prospective observational study identified 98 patients with suspected bacterial aspiration pneumonia (BAP) who underwent invasive telescopic plugged catheter (TPC) sampling followed by semi-quantitative culturing. All patients were started on broad-spectrum antibiotics pending culture results for BAP. Following TPC, 50% of the patients were found to have negative cultures, resulting in antibiotic discontinuation in two-thirds of those patients. Median duration of antibiotic was 4 days among patients determined to have non-bacterial aspiration pneumonia versus 7 days among those with bacterial pneumonia as determined by invasive sampling($p < 0.08$) suggesting the possibility of shorter duration of antibiotics with the use of invasive sampling [23••].

Advocates for non-invasive collection of the respiratory sample highlight the ease with which it can be obtained with minimal complications or cost to the patient. It is a routine procedure that is performed by the bedside nurse or the respiratory therapist [24]. Currently, conflicting data, along with institutional practices, have driven diagnostic preferences for invasive versus non-invasive sampling. While some practitioners in the USA still consider invasive sampling the "gold" standard, the 2016 American Thoracic Society/Infectious Disease Society of America (ATS/IDSA) guidelines recommend ETA as an acceptable diagnostic specimen [4]. The European Respiratory Society (ERS) 2017 guideline, however, supports obtaining distal invasive specimen for culture as it is easily accessible in most European institutions. Furthermore, the task force emphasizes that accurate identification of microbiological data could potentially result in fewer antibiotic days with narrow-spectrum coverage and that could outweigh the risk of the procedure in the appropriate patient [25, 26].

Analytical Issues: Laboratory

To implement a successful antimicrobial and diagnostic stewardship program, there needs to be a collaborative effort between health care practitioners and the clinical microbiology laboratory [27]. Ideally, the clinical microbiologist plays a vital role in guiding antibiotic selection by addressing appropriate testing criteria, specimen handling, providing timely culture data with susceptibility and guidance on accurate interpretation of the results [28]. However, the level of participation varies based on the institutional culture, availability of the microbiologist, and educational training [27].

Sample Transport and Storage

Once obtained, respiratory samples should be transported within 2 h of collection and processed at room temperature or kept at 4 °C up to 24 h if processing is to be delayed [29]. Further delay, greater than 24 h, can limit bacterial growth of certain pathogenic organisms such as *Pseudomonas aeruginosa*. In addition, freezing respiratory samples at − 80 °Celsius are not recommended because of variable results in bacterial growth which overall limits diagnostic accuracy [29]. Prompt processing of samples can minimize overgrowth of non-pathogenic organisms the presence of which can make it hard to differentiate between true colonization and infection [7••].

Timely Reporting of Culture Data

VAP requires prompt microbiological reporting for tailoring antibiotics. Semi-quantitative and quantitative cultures of the respiratory sample can take up to 48–72 h for full organism identification and susceptibility testing, whereas Gram stain smear results are usually available in 2–3 h. However, the semi-quantitative culture is able to provide additional data with designated growth thresholds differentiating pathologic organisms from simple contaminants. A few studies have compared respiratory sample Gram stain to culture results to identify quantitative thresholds that may improve the utility of the smear results. In an observational study by Shokouhi et al., the authors compared the results of the semi-quantitative culture from both the tracheal aspirate and BAL to quantitative smears. Good-quality samples (i.e., < 10 epithelial cells and > 25 neutrophils per high power field) were evaluated for the presence of organisms. Among 125 samples that were positive by semi-quantitative culturing, the mean number of organisms identified in smear was 47 ± 38 in 10 fields of optical microscopy. For samples obtained from tracheal aspirates, 35 microorganisms in 10 fields of optical microscopy had a 90% sensitivity and 91% specificity with area under receiver operating curve (AUROC) of 96% ($p < 0.001$). As expected, the smear quantitative cutoff or threshold was lower for BAL samples (relative to tracheal aspirate) with 9 microorganisms in 10 fields of optical microscopy with a sensitivity of 86.4% and specificity of 81% with AUROC of 90.5% ($p < 0.001$) [30••]. In current laboratory and clinical practice, quantitative reporting of smear Gram stains is not the standard of practice as there is no validated diagnostic cutoff for smear test results. Ultimately, the goal is to demonstrate that Gram stain smears can provide adequate guidance in expediting antibiotic stewardship. This was explored by Yashimura et al. in their retrospective study comparing a Gram stain–based algorithm to

ATS/IDSA guideline-based algorithm in their impact on antibiotic selection in patients with suspected VAP. The results of the Gram stain were reported as Gram-positive clusters or chains and Gram-negative rods. Out of 131 cases, appropriate antibiotic selection was observed in 95% of guideline-based and 92% of Gram stain-based cases ($p = 0.134$). Furthermore, there was less prescription of anti-MRSA and anti-pseudomonal antibiotics in the Gram stain algorithm compared with the guideline-based algorithm (31.3% vs 71%, $p < 0.001$ and 52 vs 70%, $p < 0.001$, respectively) [31•]. This study suggests that the Gram stain has the potential to streamline antibiotic therapy and curtail the use of broad-spectrum agents sooner than culture results.

While the correlation of Gram stains is useful and easily accessible, there has been an introduction of respiratory PCR panels that have been useful in rapidly identifying bacterial and viral pathogens [32]. These have been FDA cleared for ETA and BAL samples and raise the possibility of decreasing unnecessary antibiotic use if routinely implemented in clinical practice. Similarly, the use of the biomarker procalcitonin has been associated with reductions in antibiotic use when implemented in ICU protocols [33]. However, its utility as a diagnostic biomarker in adjunct to clinical criteria for VAP remains unclear [4]. Though further discussion of these topics is beyond the scope of this review that focuses on bacterial culturing, these are two potential tools that need to be explored in VAP diagnostic stewardship.

Post-analytical Issues: Reporting

Interpretation of Culture Data

Once the respiratory sample has been submitted, ATS/IDSA guidelines recommend initiation of empiric antibiotic therapy with activity against *Pseudomonas aeruginosa* and methicillin-resistant *Staphylococcus aureus* (MRSA) while awaiting culture data. Patient is reassessed within 48–72 h with the ultimate goal of narrowing the antibiotic selection, if possible. Current literature suggests that early discontinuation of antibiotics in the setting of negative respiratory culture is associated with lower rate of MDR superinfection without affecting overall mortality [34]. Unfortunately, limited understanding and misinterpretation of the microbiology data makes it challenging to effectively implement timely de-escalation of antibiotics [11]. Furthermore, even in the absence of MRSA or *Pseudomonas aeruginosa*, polymicrobial culture results often encourage the clinician to prescribe antibiotics [8]. In a quasi-experimental study, Musgrove et al. reported significant improvement in antibiotics use by adjusting the way respiratory cultures were reported in the electronic medical record (EMR). The authors implemented the concept of behavioral nudge to influence clinical practice. Respiratory cultures that grew respiratory flora were reported with a comment indicating the absence of MRSA and *P. aeruginosa*. In their 6-month post-intervention period, they observed an improvement in antibiotic de-escalation from 39 to 73% ($p < 0.001$) and a lower median duration of anti-pseudomonal and MRSA therapy from 7 to 5 days ($p < 0.001$). Isolation of MDR organisms in respiratory cultures also dropped from 8 to 1% between pre- and post-intervention periods ($p < 0.035$) [35••].

Another diagnostic stewardship intervention related to reporting is the restrictive release of bacterial antimicrobial susceptibility testing results [27]. Some institutions have implemented selective reporting of antimicrobial susceptibilities to encourage a more judicious use of antibiotics [27, 36]. In a study by Cunney et al., a clinical microbiology team of one consultant and two senior microbiologists was tasked with evaluating the indications for sending cultures, the clinical setting, and provide a 24-h service for clinicians requesting the release of susceptibilities and guidance on specific therapy. Specimens included sputum, urine, and soft tissue. In the setting of positive cultures, commentary was provided to contact the clinical microbiology team if considering therapy, with additional analysis to assist in differentiating colonization from pathogenic organisms. Results showed that clinicians were more likely to engage the clinical microbiology team in cases where the positive culture was reported with comments suggesting against antibiotic management (RR 2.72, 95% CI 1.15–6.48, $p = 0.03$) or if the organism was MDR (RR 3.48, 95% CI 1.87–6.48, $p < 0.001$). In addition, for those cultures where susceptibilities were released, therapy was significantly more likely to be started or altered compared with those whose susceptibilities were withheld (41% vs 22% RR 2.07, 95% CI 1.08–3.97, $p = 0.03$). Overall, prescribers were less likely to start antibiotics if information on susceptibilities was suppressed. This reinforces the notion that release of antimicrobial susceptibilities influences the decision in favor of treating. [36]. However, to successfully implement a selective release of susceptibility, there needs to be an infrastructure that would support such an endeavor. This should include guidance by clinical microbiology or infectious disease consultants and access to susceptibility results in a timely manner when those are necessary to guide patient treatment.

Summary and Future Directions

In summary, the diagnosis of VAP is challenging and reliance upon clinical features and imaging can be misleading. Nonetheless, clinical suspicion is still vital in risk stratifying the probability of true infection and along with objective data from respiratory sampling can help streamline the diagnosis of VAP and limit decision pathways that are based on pure clinical gestalt [37]. The application of a fast and frugal

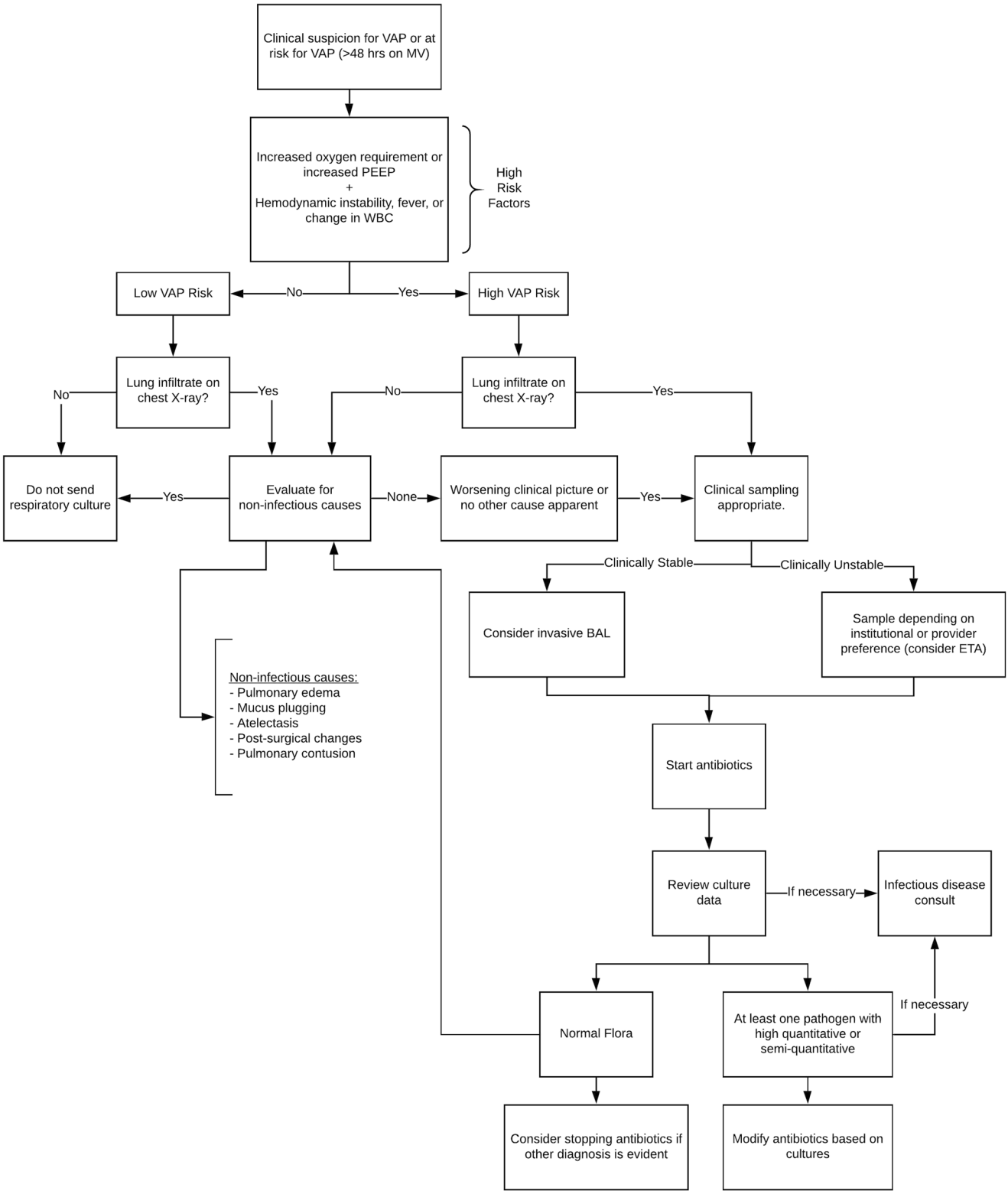

Fig. 1 Algorithic pathway for a streamlined approach for VAP diagnosis

algorithmic approach has been validated in patients with catheter-associated urinary tract infection and has shown to limit the tendency of over-culturing [38•]. We can extrapolate similar pathways to the diagnosis of VAP, with the understanding that differences in patient acuity can limit clinical application. Recommendations are summarized in Fig. 1.

There are several points in the VAP diagnostic pathway that can be targeted to ensure a more appropriate approach to

Table 2 Potential diagnostic stewardship interventions in the diagnostic pathway for ventilator-associated pneumonia (VAP)

Point of intervention	Pre-analytic	Analytic	Post-analytic	Diagnostic stewardship intervention method
VAP clinical suspicion and diagnosis	X			• Educate on difference between colonization and infection • Understand limitation of VAP guidelines • Review current physician practices
Culturing in the right clinical setting	X			• Understand VAP "mimics" • Algorithmic approach to diagnosis of ventilator related events that removes focus from routine culturing (e.g., Fig. 1)
Choosing between invasive and non-invasive respiratory tract sampling	X			• Risk-benefit of invasive vs non-invasive sampling relative to clinical suspicion and technical expertise, e.g., avoid routine non-invasive sampling with low threshold for VAP clinical suspicion
Appropriate collection and handling of specimen	X	X		• Prevent delay of sample delivery to lab
Analysis of specimen quality		X		• Rejection of poor-quality specimens
Reporting of results		X		• Reporting appropriate method of respiratory tract sampling, e.g., quantitative cultures reported only for true BAL samples
		X	X	• Interpretive reporting, e.g., commentary indicating absence of pathogens such as MRSA and *Pseudomonas*
Antimicrobial susceptibility reporting			X	• Susceptibilities performed or released only upon request

selecting patients for testing, appropriate respiratory tract sampling, and reporting of results. These include educating providers on conditions that mimic VAP, the potential for overdiagnosis in the setting of a low pre-test probability, selecting only high-risk or high pre-test probability patients for non-invasive sampling, and selective reporting of culture results and antimicrobial susceptibilities. These are summarized in Table 2, and provide an algorithmic approach to minimize unnecessary testing (Fig. 1).

Conclusion

Rising antimicrobial resistance is a concern of significance consequence that is shared by frontline clinicians and public health personnel. Efforts targeting clinician behavior on antimicrobial prescribing alone can be labor-intensive, and not effective in the setting of unnecessary positive culture results, particularly positive respiratory tract cultures in ventilated patients. However, system-wide changes that make the diagnostic approaches including laboratory reporting more appropriate can be a strong adjunct to traditional antimicrobial stewardship approaches and need to be pursued for ventilator-associated pneumonia.

Compliance with Ethical Standards

Conflict of Interest Dr. Kenaa declares that she has nothing to disclose.

Dr. Richert declares that she has nothing to disclose.

Dr. Claeys reports personal fees from Luminex Corporation, other from BioFire Diagnostics, from GenMark Diagnostics, outside the submitted work.

Ms. Shipper declares that she nothing to disclose.

Dr. O'Hara declares that she has nothing to disclose.

Dr. Sullivan declares that he has nothing to disclose.

Dr. Schrank declares that he has nothing to disclose.

Dr. Morgan reports grants from CDC, NIH, AHRQ, grants from VA HSRD, other from IDSA and SHEA for expenses to organize or present at national meetings, other from Springer Nature Inc., outside the submitted work.

Dr. Shanholtz declares that he has nothing to disclose.

Dr. Leekha reports grants from CDC and AHRQ, outside the submitted work.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

References

Papers of particular interest, published recently, have been highlighted as:

- • Of importance
- •• Of major importance

1. Ferrer M, Torres A. Epidemiology of ICU-acquired pneumonia. Curr Opin Crit Care. 2018 Oct;24(5):325–31.
2. Piriyapatsom A, Lin H, Pirrone M, De Pascale G, Corona De Lapuerta J, Bittner EA, et al. Evaluation of the infection-related ventilator-associated events algorithm for ventilator-associated pneumonia surveillance in a trauma population. Respir Care. 2016;61(3):269–76.
3. Wang Y, Eldridge N, Metersky ML, Verzier NR, Meehan TP, Pandolfi MM, et al. National trends in patient safety for four common conditions, 2005–2011. N Engl J Med. 2014;370(4):341–51.
4. Kalil AC, Metersky ML, Klompas M, Muscedere J, Sweeney DA, Palmer LB, et al. Management of adults with hospital-acquired and ventilator-associated pneumonia: 2016 clinical practice guidelines

by the Infectious Diseases Society of America and the American Thoracic Society. Clin Infect Dis. 2016 Sep 1;63(5):e61–111.
5. Dudeck MA, Weiner LM, Allen-Bridson K, Malpiedi PJ, Peterson KD, Pollock DA, et al. National Healthcare Safety Network (NHSN) report, data summary for 2012, Device-associated module Am J Infect Control 2013;
6. Browne E, Hellyer TP, Baudouin S V, Morris AC, Linnett V, McAuley DF, et al. A national survey of the diagnosis and management of suspected ventilatorassociated pneumonia. BMJ Open Respir Res [Internet]. 2014 Dec;1(1).
7.• Morgan DJ, Malani P, Diekema DJ. Diagnostic stewardship - leveraging the laboratory to improve antimicrobial use. JAMA - Journal of the American Medical Association. 2017; **This editorial discusses the importance of engaging the laboratory to ensure culture testing in the right pre-test probability. It also highlights the role of collection, processing, and reporting of the sample play a role in appropriate treatment of infections.**
8. Nussenblatt V, Avdic E, Berenholtz S, Daugherty E, Hadhazy E, Lipsett PA, et al. Ventilator-associated pneumonia: overdiagnosis and treatment are common in medical and surgical intensive care units. Infect Control Hosp Epidemiol. 2014 Mar;35(3):278–84.
9. Baur D, Gladstone BP, Burkert F, Carrara E, Foschi F, Döbele S, et al. Effect of antibiotic stewardship on the incidence of infection and colonisation with antibiotic-resistant bacteria and Clostridium difficile infection: a systematic review and meta-analysis. Lancet Infect Dis. 2017;17(9):990–1001.
10. Sarg M, Waldrop GE, Beier MA, Heil EL, Thom KA, Preas MA, et al. Impact of changes in urine culture ordering practice on antimicrobial utilization in intensive care units at an Academic Medical Center. Infect Control Hosp Epidemiol. 2016;37(4):448–54.
11. Bashir A, Gray J, Bashir S, Ahmed R, Theodosiou E. Critical points in the pathway of antibiotic prescribing in a children's hospital: the Antibiotic Mapping of Prescribing (ABMAP) study. J Hosp Infect [Internet]. 2018;44:1–6.
12. Barlam TF, Cosgrove SE, Abbo LM, Macdougall C, Schuetz AN, Septimus EJ, et al. Executive summary: implementing an antibiotic stewardship program: guidelines by the infectious diseases society of America and the society for healthcare epidemiology of America. Clin Infect Dis. 2016.
13. Quick JA, Breite MD, Barnes SL. Inadequacy of algorithmic ventilator-associated pneumonia diagnosis in acute care surgery. Am Surg. 2018;84(2):300–4.
14. Bello G, Pennisi MA, Di Muzio F, De Pascale G, Montini L, Maviglia R, et al. Clinical impact of pulmonary sampling site in the diagnosis of ventilator-associated pneumonia: a prospective study using bronchoscopic bronchoalveolar lavage. J Crit Care. 2016 Jun;33:151–7.
15. Chao WC, Chang WL, Wu CL, Chan MC. Using objective fluid balance data to identify pulmonary edema in subjects with ventilator-associated events. Respir Care. 2018 Aug 7;
16. Shan J, Chen HL, Zhu JH. Diagnostic accuracy of clinical pulmonary infection score for ventilator-associated pneumonia: a meta-analysis. Respir Care. 2011 Aug;56(8):1087–94.
17. Group CCCT. A randomized trial of diagnostic techniques for ventilator-associated pneumonia. N Engl J Med. 2006;355(25): 2619–30.
18. Fagon JY, Chastre J, Wolff M, Gervais C, Parer-Aubas S, Stéphan F, et al. Invasive and noninvasive strategies for management of suspected ventilator-associated pneumonia. A randomized trial. Ann Intern Med [Internet]. 2000;132(8):621–30.
19. Solé Violán J, Fernández JA, Benítez AB, Cardeñosa Cendrero JA, Rodríguez de C. Impact of quantitative invasive diagnostic techniques in the management and outcome of mechanically ventilated patients with suspected pneumonia. Crit Care Med [Internet] 2000;28(8):2737–2741.
20. Ruiz M, Torres A, Ewig S, Marcos MA, Alcón A, Lledó R, et al. Noninvasive versus invasive microbial investigation in ventilator-associated pneumonia: evaluation of outcome. Am J Respir Crit Care Med [Internet]. 2000;162(1):119–25.
21. Sanchez-Nieto JM, Torres A, Garcia-Cordoba F, El-Ebiary M, Carrillo A, Ruiz J, et al. Impact of invasive and noninvasive quantitative culture sampling on outcome of ventilator-associated pneumonia: a pilot study. Am J Respir Crit Care Med [Internet]. 1998;157(2):371–6.
22. Berton DC, Kalil AC, Teixeira PJZ. Quantitative versus qualitative cultures of respiratory secretions for clinical outcomes in patients with ventilator-associated pneumonia. Cochrane Database of Systematic Reviews. 2014.
23.•• Lascarrou JB, Lissonde F, Le Thuaut A, Bachoumas K, Colin G, Henry Lagarrigue M, et al. Antibiotic therapy in comatose mechanically ventilated patients following aspiration: differentiating pneumonia from pneumonitis. Crit Care Med [Internet]. 2017;45(8): 1268–1275. **In this prospective observational study, investigators highlight the challenge in clinically differentiating bacterial aspiration pneumonia from non-bacterial aspiration pneumonitis. With invasive respiratory sampling, it is possible to get culture data that can guide in early discontinuation of empiric antibiotics.**
24. Frota OP, Ferreira AM, Barcelos L, da Watanabe SE, Carvalho NCP, Rigotti MA. Collection of tracheal aspirate: safety and microbiological concordance between two techniques TT - Colheita de aspirado traqueal: segurança e concordância microbiológica entre duas técnicas TT - Recolección de aspirado traqueal: seguridad y concordanci. Rev da Esc Enferm da USP [Internet]. 2014;48(4): 618–24.
25. Torres A, Niederman MS, Chastre J, Ewig S, Fernandez-Vandellos P, Hanberger H, et al. International ERS/ESICM/ESCMID/ALAT guidelines for the management of hospital-acquired pneumonia and ventilator-associated pneumonia. Eur Respir J [Internet]. 2017 Sep;50(3).
26. Schnabel RM, van der Velden K, Osinski A, Rohde G, Roekaerts PM, Bergmans DC. Clinical course and complications following diagnostic bronchoalveolar lavage in critically ill mechanically ventilated patients. BMC Pulm Med. 2015;15:101–7.
27. Morency-Potvin P, Schwartz DN, Weinstein RA. Antimicrobial stewardship: how the microbiology laboratory can right the ship. Clin Microbiol Rev. 2017;30(1):381–407.
28. Bouza E, Muñoz P, Burillo A. Role of the clinical microbiology laboratory in antimicrobial stewardship. Medical Clinics of North America. 2018.
29. Kneidinger N, Warszawska J, Schenk P, Fuhrmann V, Bojic A, Hirschl A, et al. Storage of bronchoalveolar lavage fluid and accuracy of microbiologic diagnostics in the ICU: a prospective observational study. Crit Care [Internet]. 2013;17(4).
30.•• Shokouhi S, Darazam IA, Sadeghi M, Gachkar L, Dolatshahi S. Diagnostic yield of a direct quantitative smear of lower respiratory tract secretions in patients with suspected pneumonia compared with a semi-quantitative culture. Tanaffos. 2017;16(1):9–12. **In this prospective study, investigators evaluated how Direct Quantitative Smear with proper staining maybe an easy, cost-effective, and rapid method. They compared respiratory sample from BAL and endotracheal aspirate to identify a 35 microorganisms in10 HPF of microscopy was the ideal cutoff. Though still novel and difficult to apply for different microorganisms and in different laboratory settings, this approach could be investigated further as a way to quickly identify the absence of pathogenic organisms and discontinue antibiotics earlier.**
31.• Yoshimura J, Kinoshita T, Yamakawa K, Matsushima A, Nakamoto N, Hamasaki T, et al. Impact of Gram stain results on initial treatment selection in patients with ventilator-associated pneumonia: a

retrospective analysis of two treatment algorithms. Crit Care [Internet]. 2017;21(1) **In this study, investigators wanted to evaluate if bedside Gram stain of endotracheal aspirates could be used to determine appropriate initial antimicrobial therapy for VAP as compared with ATS/IDSA guidelines algorithmic approach.**

32. Sullivan KV, Dien BJ. New and novel rapid diagnostics that are impacting infection prevention and antimicrobial stewardship. Curr Opin Infect Dis [Internet]. 2019;32:–1.
33. Rhee C. Using procalcitonin to guide antibiotic therapy. Open Forum Infect Dis. 2017;4(1):1–10.
34. Raman K, Nailor MD, Nicolau DP, Aslanzadeh J, Nadeau M, Kuti JL. Early antibiotic discontinuation in patients with clinically suspected ventilator-associated pneumonia and negative quantitative bronchoscopy cultures. Crit Care Med. 2013;41(7):1656–63.
35.•• Musgrove MA, Tibbetts R, Peters M, Samuel L, Davis SL, Kendall RE, et al. Microbiology comment nudge improves pneumonia prescribing. Open Forum Infect Dis. 2018;5(7):1–5 **In this single pre and post quasi experimental study, investigators enrolled two hundred and ten patients who were treated with anti-MRSA and anti-pseudomonal antibiotics for respiratory infections. Reporting of cultures for patients without dominant organisms were labeled as "commensal respiratory flora only: no S.aureus/MRSA or P.aeroginosa." In the post intervention group, there was a 5.5 increased odds of antibiotic de-escalation.**
36. Cunney R. Interpretative reporting and selective antimicrobial susceptibility release in non-critical microbiology results. J Antimicrob Chemother. 2002;45(5):705–8.
37. Klompas M, Kleinman K, Khan Y, Evans RS, Lloyd JF, Stevenson K, Samore M, Platt R, CDC Prevention Epicenters Program. Rapid and reproducible surveillance for ventilator-associated pneumonia. Clin Infect Dis 2012;54(3):370–377.
38.• Naik AD, Skelton F, Amspoker AB, Glasgow RA, Trautner BW. A fast and frugal algorithm to strengthen diagnosis and treatment decisions for catheter-associated bacteriuria. PLoS One. 2017;12(3) **Improving the diagnostic and treatment accuracy for CAUTI by implementing a fast and frugal algorithm results in the reduction of overtreatment of asymptomatic bacteruria**.

Affiliations

Blaine Kenaa[1] · Mary Elizabeth Richert[2] · Kimberly C. Claeys[3] · Andrea Shipper[4] · Kaede V. Sullivan[5] · Gregory M. Schrank[6] · Lyndsay M. O'Hara[7] · Daniel J. Morgan[7] · Carl Shanholtz[1] · Surbhi Leekha[7]

[1] Department of Medicine, Department of Pulmonary and Critical Care, University of Maryland School of Medicine, 110 S. Paca st. Second floor pulmonary, Baltimore, MD 21201, USA

[2] Division of Internal Medicine, PGY-3, Department of Medicine, University of Maryland School of Medicine, University of Maryland Medical Center, N3W42, 22 S. Greene Street, Baltimore, MD 21201, USA

[3] Infectious Diseases, Department of Pharmacy Practice and Science, University of Maryland School of Pharmacy, 20 N. Pine Street, Baltimore, MD 21201, USA

[4] Health Sciences and Human Services Library, University of Maryland Baltimore, 601 W. Lombard St., Baltimore, MD 21201, USA

[5] Pathology and Laboratory Medicine, Medicine Education and Research Building, Lewis Katz School of Medicine, 3500 N. Broad St., Philadelphia, PA 19140, USA

[6] Division of Infectious Diseases, Department of Medicine, University of Maryland School of Medicine, University of Maryland Medical Center, N3W42, 22 S. Greene Street, Baltimore, MD 21201, USA

[7] Department of Epidemiology and Public Health, University of Maryland School of Medicine, 685 W. Baltimore Street, Baltimore, MD 21201, USA