



Fig. 1. Antimicrobial consumption relative to COVID-19 admissions from September 2018 to August 2021. The left y-axis represents days of therapy per 1,000 patient days (DOT per 1,000 PD) for antibiotics and total COVID-19 admissions for the respective variables. $PoCC = \frac{[(meropenem\ DOT\ per\ 1,000\ PD)]}{[(meropenem\ DOT\ per\ 1,000\ PD + cefepime\ DOT\ per\ 1,000\ PD + piperacillin-tazobactam\ DOT\ per\ 1,000\ PD)]}$

for multiple comparisons was utilized to determine significance with an initial baseline α of 0.05. All data analyses were performed using R software (R Foundation for Statistical Computing, Vienna, Austria, 2021). **Results:** Normality was evaluated with QQ-plots and all data demonstrated normality. Bonferroni correction produced an adjusted α value of 0.007. We detected significant increases in the use of cefepime, piperacillin-tazobactam, ceftriaxone, and azithromycin following the onset of the COVID-19 pandemic. We noted a significant decrease in the PoCC metric during this period. No significant change was noted for levofloxacin or meropenem. **Conclusions:** The COVID-19 pandemic produced significant changes in antimicrobial use patterns at our institution. We noted statistically significant increases in bacterial community-acquired pneumonia-focused antibiotics (ceftriaxone and azithromycin). We observed significant increases for cefepime and piperacillin-tazobactam. Interestingly, relative utilization of carbapenems as measured by the PoCC metric continued to decrease during this time. This trend was primarily driven by increases in cefepime and piperacillin-tazobactam utilization while meropenem utilization remained relatively constant. This study highlights the importance of looking at normalized antibiotic consumption data and not relative-use data alone.

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Subject Category: Antibiotic Stewardship

Recommendations for antimicrobial stewardship during end-of-life patient care

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Background: Antimicrobials are frequently used during end-of-life care and may be prescribed without a clear clinical indication. Overuse of antimicrobials is a major public health concern because of the development of multidrug resistant organisms (MDROs). Antimicrobial stewardship programs are associated with reductions in antibiotic resistance and antibiotic-associated adverse events. We sought to identify and describe opportunities to successfully incorporate stewardship strategies into end-of-life care. **Methods:** We completed semistructured interviews with 15 healthcare providers at 2 VA medical centers, 1 inpatient setting and 1 long-term care setting. Interviews were conducted via telephone between November 2020 and June 2021 and covered topics related to antibiotic prescribing for hospice and palliative-care patients, including how to improve antimicrobial stewardship during the end-of-life period. We targeted healthcare providers who are involved in prescribing antibiotics during the end-of-life period, including hospitalists, infectious disease physicians, palliative care and hospice physicians, and pharmacists. All interviews were recorded,

transcribed, and analyzed using consensus-based inductive and deductive coding. **Results:** End-of-life care, particularly hospice care, was described as an underutilized resource for patients, who are often enrolled in their final days of life rather than earlier in the dying process. Even at facilities with established antimicrobial stewardship programs, healthcare providers interviewed believed that opportunities for antimicrobial stewardship in the hospice and palliative care settings were missed. Recommendations for how stewardship should be incorporated in end-of-life care included receiving feedback on antimicrobial prescribing, increasing pharmacist involvement in prescribing decisions, and targeted education for providers on end-of-life care, including the value of shared decision making with patients around antibiotic use. **Conclusions:** Improved antibiotic prescribing during end-of-life care is critical in the effort to combat antimicrobial resistance. Healthcare providers discussed antimicrobial stewardship activities during end-of-life patient care as a potential avenue to improve appropriate antibiotic prescribing. Future research should evaluate the feasibility and effectiveness of incorporating these strategies into end-of-life patient care.

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Assessment of antibiotic appropriateness in hospitalized veterans with COVID-19 in the VA MidSouth Healthcare Network (VISN9)

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Background: Bacterial coinfections with COVID-19 appear to be rare, yet antibiotic use in this population is high. Limited guidance is available regarding the use of antibiotics in these patients. In response, a multidisciplinary group of physicians and pharmacists from 5 VISN9 facilities developed a guideline for the use of antibiotics with COVID-19 in July 2021. This guideline created a network-wide standard for antibiotic use and facilitates the assessment of antibiotic appropriateness in hospitalized veterans with COVID-19. **Methods:** In this observational, cross-sectional study, we reviewed veterans diagnosed with COVID-19 from August 1 through September 30, 2021, who were admitted to VISN9 facilities. Use of antibiotics was assessed during the first 4 days of admission. If antibiotics were prescribed, their use was determined to be appropriate or inappropriate based on the presence or absence of a finding concerning for bacterial coinfection as outlined in the guideline (Table 1). Additional data including procalcitonin results as well as positive sputum cultures were collected. **Results:** In total, 377 veterans were admitted for COVID-19 during the study period. Among them, 42 veterans (11%) received antibiotics for nonrespiratory infections and were removed from this analysis. Of the remaining 335 veterans, 229 (68%) received antibiotics and 116 (51%) of those met guideline criteria that were concerning for bacterial coinfection. Additionally, 32 (14%) of the 229 veterans who received antibiotics had >1 finding concerning for bacterial coinfection. Procalcitonin levels were obtained in 97 (42%) of 229. Only 33 veterans (14%) who received antibiotics had an elevated procalcitonin, and only 19 (8%) had a positive sputum culture. **Conclusions:** Antibiotic use was common in hospitalized veterans with COVID-19 in VISN9 facilities. This results are comparable to findings in the published literature. Among those receiving antibiotics

Table 1. Findings concerning for bacterial co-infection in patients with COVID-19

Any of the following:
Elevated leukocyte count
Unilateral lobar consolidation on chest imaging
Recrudescence of fever after initial defervescence
Septic Shock

early in their hospitalization, half were considered appropriate based on our guideline. Quality improvement initiatives are needed to improve implementation of the network guideline to reduce the overuse of antibiotics for management of COVID-19. Additionally, procalcitonin may be a helpful tool for hospitalized veterans with COVID-19.

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Assessing the association between cefepime percentage free trough level and neurotoxicity

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Background: Cefepime has a known association with neurotoxicity due to its ability to cross the blood–brain barrier. The symptoms of neurotoxicity are highly variable. It has been postulated that cefepime neurotoxicity is associated with elevated levels of the drug. However, studies assessing for an association between serum drug level and the incidence of neurotoxicity have yet to establish a consistent threshold. We assessed serum cefepime levels and incidence of neurotoxicity to help develop a dosing strategy to minimize adverse effects. **Method:** In total, 32 inpatients admitted from January 2019 to November 2021 who received cefepime according to institutional standard dosing regimens for at least 72 hours were reviewed by infectious diseases pharmacists who obtained serum cefepime

levels and performed pharmacokinetic analyses to obtain percentage free trough levels. Cefepime percentage free trough levels were defined as therapeutic if they were above the known minimum inhibitory concentration (MIC) of the treated organism and were <40 µg/mL. Patient charts were reviewed for clinical findings consistent with cefepime-induced neurotoxicity. Numerical and statistical analyses were performed to assess factors with a significant association with neurotoxicity. **Results:** Overall, 16 (47.1%) patients showed some evidence of neurotoxicity, 9 (56.3%) of whom had a likely alternate clinical cause of symptoms (Table 1). We did observe that patients with creatinine clearance <60 mL/min were more likely to have symptoms concerning for neurotoxicity. **Conclusions:** Cefepime percentage free trough levels were highly variable, and no association with neurotoxicity was observed. Patients with decreased creatinine clearance were significantly more likely to develop neurologic findings consistent with cefepime-induced neurotoxicity. Further study is needed to establish a relationship between cefepime pharmacokinetic values and incidence of neurotoxicity.

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Implementing Leading antimicrobial stewardship practices in United States hospitals – A qualitative study

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Background: In May 2018, The Joint Commission, The Pew Charitable Trusts, and the CDC cosponsored a meeting of experts who identified 6 evidence-based leading practices that antimicrobial stewardship programs (ASPs) should be doing beyond having basic infrastructure for improving antibiotic prescribing. The Joint Commission Department of Research working with external experts in 2020 conducted a prevalence study to assess what proportion of Joint Commission-accredited hospitals had implemented the 6 leading practices identified (results presented at SHEA Spring 2021). In this qualitative study, we collected information about how hospitals implemented ASP leading practices to identify facilitators and barriers to implementation among diverse hospitals. **Methods:** We conducted in-depth telephone interviews with a subset of ASP leaders from hospitals that participated in the 2020 prevalence study. We used purposive sampling to select 30 hospitals from 288 hospitals based on leading practices implemented, hospital size, and system membership. An experienced qualitative researcher (M.K.) not previously affiliated with the Joint Commission interviewed all participants using a semistructured interview guide. The framework method of analysis was used to review and organize data. We used the constant comparative approach to ensure that factors were not missed. Each transcript was reviewed by at least 2 researchers who compared coded findings in group discussion sessions. Two researchers independently identified key factors and combined findings following discussion and review. We focused on super factors that are relevant to implementing multiple leading practices. **Results:** ASP leaders from 30 hospitals were interviewed. Participating hospitals were evenly distributed across hospital size (10 small, 10 medium, 10 large) and membership in a health system (16 system, 14 nonsystem). At least 14, (46.7%) interviewees had pharmacist in their title; 11 (36.7%) had pharmacist-antimicrobial stewardship; and 5 (16.6%) had other titles (eg, infection preventionist). Super factors included ASP team capacity, ID expertise, having a physician champion, relationships with clinicians and relevant departments, structure of electronic health records, adequate software, and information technology resources. Small and rural nonsystem hospitals often lacked

Table 1. Distribution of Neurotoxicity with Cefepime Percent Free Trough

CrCl (mL/min)		N = neurologic symptoms reported (median percent free trough, µg/mL)	N = likely alternate explanation for neurotoxicity	N = no neurotoxicity (median percent free trough, µg/mL)
>90	Subtherapeutic	0	0	0
	Therapeutic	4 (16.1)	1	7 (11.5)
	Supratherapeutic	2 (60.15)	2	3 (52.8)
60-90	Subtherapeutic	0	0	1 (1.8)
	Therapeutic	3 (2.6)	2	3 (21.4)
	Supratherapeutic	3 (67.6)	2	2 (76.9)
30-59	Subtherapeutic	0	0	0
	Therapeutic	1 (27.9)	1	0
	Supratherapeutic	0	0	0
≤30	Subtherapeutic	0	0	0
	Therapeutic	1 (35.4)	1	0
	Supratherapeutic	2 (78.4)	0	0

Table 2. Patient Characteristic and Cefepime Level Distribution

	Total patients (N = 32)	N = subtherapeutic (median percent free trough, µg/mL)	N = therapeutic (median percent free trough, µg/mL)	N = supratherapeutic (median percent free trough, µg/mL)
Age (years)				
≤40	10	0	6 (7.7)	4 (54.05)
41-64	10	0	8 (21.05)	2 (49.0)
≥65	12	1 (1.8)	5 (9.3)	6 (72.5)
Sex				
Male	16	0	11 (7.7)	5 (76.6)
Female	16	1 (1.8)	8 (19.8)	7 (53.6)
Weight (adjusted, kg)				
≤50	2	0	0	2 (78.4)
51-70	12	1 (1.8)	8 (22.95)	3 (53.6)
71-90	16	0	10 (9.6)	6 (54.05)
≥90	2	0	1 (38.3)	1 (67.6)
CrCl (mL/min)				
>90	16	0	11 (11.5)	5 (53.6)
60-90	12	1 (1.8)	6 (8.35)	5 (67.6)
30-59	1	0	1 (27.9)	0
≤30	3	0	1 (35.4)	2 (78.4)