Effect of Antimicrobial Stewardship Program Guidance on the Management of Uncomplicated Skin and Soft Tissue Infections in Hospitalized Adults

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Abstract

Objective: To assess the effect of an antimicrobial stewardship program (ASP)—bundled initiative on the appropriate use of antibiotics for uncomplicated skin and soft tissue infections (uSSTIs) at 2 academic medical centers in Pittsburgh, Pennsylvania.

Patients and Methods: A retrospective preintervention and postintervention study was conducted to compare management of patients admitted with uSSTIs before and after the implementation of the bundled initiative. The preintervention period was from August 1, 2014, through March 31, 2015, and the postintervention period was from August 1, 2015, through March 31, 2016.

Results: A total of 160 patients were included in the preintervention cohort, and 163 were included in the postintervention cohort. Compared with the preintervention group, the mean duration of therapy decreased (12.5 days vs 8.8 days; *P* < .001) and an appropriate duration of less than 10 days increased in more patients (20.6% [33 of 160] vs 68.7% [112 of 163]; *P* < .001) in the postintervention period. Fewer patients were exposed to antimicrobials with extended gram-negative (44.4% [71 of 160] vs 9.2% [15 of 163]; *P* < .001), anaerobic (39.4% [63 of 160] vs 9.8% [16 of 163]; *P* < .001), and antipseudomonal (16.3% [26 of 160] vs 1.8% [3 of 163]; *P* < .001) coverage. The mean length of stay decreased from 3.6 to 2.2 days (*P* < .001) without an increase in 30-day readmissions (6.3% [10 of 160] vs 4.9% [8 of 163]; *P* = .64). The ASP made recommendations for 125 patients, and 96% were accepted.

Conclusion: Implementation of an ASP-bundled approach aimed at optimizing antibiotic therapy in the management of uSSTIs led to shorter durations of narrow-spectrum therapy as well as shorter hospital length of stay without adversely affecting hospital readmissions.

In patients with uncomplicated SSTIs (uSSTIs), 5 to 7 days of antibiotic therapy has been shown to be effective for clinical cure.6-9 However, treatment duration at our institutions and other centers is often inappropriately long, with courses commonly prescribed up to or beyond 2 weeks.10-12 In addition, aerobic
gram-positive organisms, namely, *Staphylococcus aureus* and β-hemolytic streptococcal species, are the predominant etiologic pathogens in uSSTIs.\(^1\)\(^0\)\(^1\)\(^3\)\(^-\)\(^2\)\(^0\) Regardless, patients are frequently treated with broad-spectrum antibiotic therapy with activity against aerobic gram-negative and anaerobic bacteria.\(^1\)\(^0\)\(^-\)\(^1\)\(^2\) The appropriate use of antimicrobials is critical, as unnecessary use is associated with patient harm due to increased drug resistance, adverse drug events and toxicity, and collateral damage including *Clostridium difficile* infection.\(^2\)\(^1\)\(^-\)\(^2\)\(^9\) Therefore, reducing the duration of antibiotic therapy and minimizing the use of broad-spectrum therapy represent ideal opportunities to reduce unnecessary antibiotic exposure in hospitalized patients with uSSTIs.

To improve antibiotic use in cases of uSSTIs, our antimicrobial stewardship program (ASP) developed a syndrome-specific bundled intervention as described in the Methods section. The aims of this intervention were to (1) reduce the duration of therapy, (2) reduce the use of antibiotic agents with extended gram-negative and anaerobic coverage, and (3) shorten the hospital length of stay for patients admitted with uSSTIs. In this study, we assessed the effect of this ASP intervention at 2 large teaching facilities.

**PATIENTS AND METHODS**

**Study Setting**

Allegheny General Hospital (AGH) is a 631-bed quaternary care teaching facility with approximately 22,000 inpatient admissions yearly. The Western Pennsylvania Hospital (WPH) is a 317-bed community-based teaching hospital with nearly 6800 inpatient admissions annually. Both facilities are located in Pittsburgh, Pennsylvania, and are members of the Allegheny Health Network. The evaluation was approved and granted exempt status from the institutional review board of the Allegheny Health Network, as it was deemed quality assessment and quality improvement.

**Study Design**

We conducted a retrospective preintervention and postintervention study comparing the management of patients admitted with uSSTIs before and after the implementation of an ASP-bundled initiative. The preintervention period was from August 1, 2014, through March 31, 2015, and the postintervention period was from August 1, 2015, through March 31, 2016. The findings from the preintervention period have been previously published.\(^1\)\(^2\)

** Intervention**

After review of the preintervention management of patients admitted with uSSTIs at AGH and WPH, considerable opportunities were exposed to improve antibiotic use. Our ASP assembled a multidisciplinary task force to create a clinical decision-making algorithm for the evaluation and management of SSTIs, which focused primarily on uSSTIs (Supplemental Figure, available online at http://www.mcpiqojournal.org). For uSSTIs, we recommended against the use of routine plain films, advanced imaging modalities, blood cultures, serum erythrocyte sedimentation rate, and serum C-reactive protein level. The use of agents with extended gram-negative or anaerobic coverage was specifically discouraged. For patients with nonpurulent uSSTIs, intravenous cefazolin was recommended for empirical therapy. For patients with uSSTIs associated with purulence, we recommended empirical intravenous vancomycin, performing incision and drainage, and obtaining wound gram stain and culture. The recommended total duration of therapy was 7 days for those patients with uSSTIs who experienced improvement within 48 to 72 hours. Adjunct therapy with a nonsteroidal anti-inflammatory agent for 5 days was recommended, unless contraindicated. Elevation of the affected limb for all cases and evaluation for and treatment of tinea pedis for cases involving the lower extremities was also recommended. To ensure adherence to the clinical decision-making algorithm, we used a 3-pronged bundled approach:

1. **Dissemination of the clinical decision-making algorithm** to all medical and house staff via e-mail and as part of our yearly antimicrobial guide (available in print and on our network’s intranet). Laminated copies were posted at nursing units, physician work areas, and the internal medicine residency department.

2. **Educational lectures** were presented to internal medicine residency house staff, Internal Medicine medical staff, the Department of Hospitalist Medicine, and the Division of Infectious Diseases.
3. Prospective audit with real-time intervention and feedback was conducted on patients identified by the ASP as having a potential opportunity for improvement in management. During the postintervention period, the ASP reviewed patients hospitalized with a primary admission diagnosis of SSTIs through use of the electronic health record Monday through Friday. The ASP contacted the primary service via phone call or secure text page to discuss management and provide feedback.

Data Collection
For the preintervention period, we included all patients with a primary diagnosis of SSTI using International Classification of Diseases, Ninth Revision (ICD-9), coding data. The search codes included cellulitis and cutaneous abscess (code 681), other cellulitis and abscess (code 682), acute lymphadenitis (code 683), other infections of skin and subcutaneous tissue (code 686), and erysipelas (code 683). These data were electronically extracted by our quality intelligence department. For the postintervention period, we included all patients evaluated by our ASP who were admitted with a primary diagnosis for cellulitis, cutaneous abscess, acute lymphadenitis, and erysipelas. In addition, in this period, we identified all patients with a primary diagnosis of SST1 using ICD-9 and International Classification of Diseases, Tenth Revision (ICD-10) coding data, as ICD-10 went into effect on October 1, 2015. The ICD-10 search codes included cellulitis and acute lymphangitis (code L03), acute lymphadenitis (code L04), other local infections of skin and subcutaneous tissue (code L08), and erysipelas (code A46).

For patients with multiple hospitalizations at AGH and WPH for SSTI during the study period, only the original admission was reviewed and subsequent admissions were excluded. Demographic information, admission and discharge dates, and length of hospitalization were electronically extracted by our quality intelligence department. We verified the discharge diagnosis and obtained information on patient comorbidities, microbiological data, radiographic studies, inpatient and outpatient antimicrobial therapy, and subsequent inpatient clinical encounters at AGH and WPH during the 30 days after hospital discharge via review of the electronic health record by using a standardized data collection instrument.

Patients were excluded for the following reasons: age less than 18 years, transfer from an outside hospital, left against medical advice, death during index hospitalization.
an alternative concomitant bacterial infection that required antibiotic therapy, neutropenia, severe cell-mediated immunodeficiency, and complicated SSTI, defined as management in an intensive care unit, perirectal involvement, periorbital involvement, associated with human or animal bite, odontogenic source of infection, associated with diabetic ulceration or chronic underlying ulceration, surgical wound infection, traumatic amputectomy, associated with intravenous illicit drug use, concern for necrotizing infection, associated with osteomyelitis, presence of retained infected foreign body, or presence of bacteremia with an organism not deemed to be a contaminant.

### Study Definitions

The primary outcome was to determine the effect of the ASP-bundled intervention on the appropriateness of antibiotic treatment duration for uSSTIs. A treatment duration of more than 10 days was defined as inappropriate. \(^{10,30-32}\) Duration of therapy was defined as the number of calendar days during which an antibiotic was administered in the inpatient setting and prescribed to be administered on discharge from the hospital.

Secondary outcomes included the effect of the ASP-bundled intervention on the appropriateness of antibiotic selection, duration of inpatient length of stay, and all-cause rehospitalization as well as rehospitalization for SSTI to AGH or WPH within 30 days of discharge from the index admission. The use of antibiotics with extended gram-negative, extended anaerobic, and antipseudomonal activity was defined as inappropriate if they were administered for more than 24 hours.

Organisms (excluding coagulase-negative staphylococci, diphtheroids, \textit{Micrococcus}, and \textit{Propionibacterium acnes}) were considered to be the etiology of purulent SSTIs when cultured from purulent drainage, an abscess cavity, or deep tissue specimen. As needle aspirates and punch biopsies are not routinely performed for cellulitis at AGH or WPH, cases of nonpurulent SSTIs were not included in the evaluation of microbiologic etiology.

Antibiotics with extended gram-negative activity included aztreonam; colistin; tigecycline; third-, fourth-, fifth-generation cephalosporins; β-lactam/β-lactamase inhibitor combinations; carbapenems; and fluoroquinolones. Antibiotics with extended anaerobic activity included β-lactam/β-lactamase inhibitor combinations, carbapenems, metronidazole,
and tigecycline. Antibiotics with antipseudomonal activity included aztreonam, cefepime, ceftazidime, ciprofloxacin, colistin, levofloxacin, meropenem, and piperacillin/tazobactam.

Severe immunodeficiency was defined as use of long-term immunosuppressive therapy at the time of admission (equivalent of >10 mg prednisone daily), human immunodeficiency virus with a CD4 cell count of less than 350 cells/mm³, active malignant neoplasm with receipt of systemic chemotherapy within the 30 days before index admission, or receipt of previous solid organ transplant or hematopoietic stem cell transplant.

Statistical Analyses
Differences in continuous variables between the preintervention and postintervention cohorts were assessed using the 2-sample t test. A P value of less than .05 was considered statistically significant. Differences in categorical variables between the 2 cohorts were assessed using the Fisher exact test. A P value of less than .05 was considered statistically significant. We used Stata version 12 (StataCorp LLC) for statistical analyses.

RESULTS
During the preintervention and postintervention periods, respectively, 284 and 293 patients with a principal diagnosis of SSTI were initially identified by ICD-9 and ICD-10 codes (Figure 1). The final preintervention cohort included 160 patients, and the postintervention cohort included 163 patients. The cohorts had similar demographic and clinical characteristics (Table 1). The leg was the predominant site of infection. Most patients in each cohort did not have purulence associated with their uSSTIs. Among patients with associated purulence in each cohort, *Staphylococcus aureus* was the most commonly isolated organism (Figure 2).

The use of plain films and advanced imaging techniques with computed tomography and magnetic resonance imaging was similar between the 2 cohorts. Blood cultures were also obtained with similar frequency (Table 2).

The mean duration of total antibiotic therapy decreased from 12.5±3.8 days in the preintervention cohort to 8.8±2.2 days in the postintervention cohort (P <.001). The percentage of patients who received an appropriate total duration of therapy of less than 10 days increased in the postintervention period (20.6% [33 of 160] vs 68.7% [112 of 163]; P <.001), whereas the percentage of those patients who received prolonged duration of antibiotic therapy for more than 14 days decreased significantly during the postintervention period (27.5% [44 of 160] vs 0.6% [1 of 163]; P <.001) (Table 3). The use of antibiotic agents with extended gram-negative activity decreased substantially (44.4% [71 of 160] vs 9.2% [15 of 163]; P <.001) as did the use of agents with extended anaerobic activity (39.4% [63 of 160] vs 9.8% [16 of 163]; P <.001) and agents with antipseudomonal coverage (16.3% [26 of 160] vs 1.8% [3 of 163]; P <.001) (Table 3).

The mean hospital length of stay decreased from 3.6±2.5 days in the preintervention period to 2.2±1.3 days in the postintervention cohort (P <.001). A nonsignificant reduction was found in the postintervention period for all-cause 30-day readmissions (6.3% [10 of 160] vs 4.9% [8 of 163]; P = .64) and for
30-day readmissions due to recurrent infection (3.8% [6 of 160] vs 1.8% [3 of 163]; \( P = .22 \)).

In the postintervention period, our ASP evaluated 131 of 163 patients (80.4%) and made recommendations for 125 of these patients. In these 125 patients in whom ASP recommendations were made, 96% (120 of 125) were accepted by the medical teams.

**DISCUSSION**

Our ASP-bundled intervention to optimize antibiotic use in the management of uSSTIs was associated with changes in prescribing practices, including marked reduction in total duration of antibiotic therapy. In addition, our syndrome-specific approach was associated with significant reduction in the use of antibiotic agents with extended gram-negative, extended anaerobic, and antipseudomonal coverage. The interventions were also associated with substantially shorter hospital length of stay. Despite decreased antibiotic duration, spectrum, and hospital length of stay, there was no increase in 30-day readmissions.

Despite previous evidence indicating that uSSTIs can be effectively treated with shorter 5- to 7-day courses of therapy,\(^6,8,9,33\) real-world evaluations have revealed that the duration of antimicrobial therapy for hospitalized patients with cellulitis and cutaneous abscess approaches 2 weeks.\(^10-12\) The duration of therapy is prolonged despite the Infectious Diseases Society of America (IDSA) guidelines recommending 5 days of therapy.\(^1\) Our intervention was associated with a 29% reduction in duration of total therapy. The 3.7-day reduction in mean duration of therapy for the 163 patients in our postintervention cohort equates to 603 fewer days of antibiotics.

In addition, the IDSA practice guidelines for the diagnosis and management of SSTIs recommend the use of narrow-spectrum antibiotics targeting only gram-positive pathogens for cases of uSSTIs.\(^7\) Despite this, we previously reported that nearly half our patients hospitalized with uSSTIs still received inappropriate therapy with extended gram-negative coverage and a similar number received extended anaerobic coverage.\(^12\) In our study, our ASP initiatives were associated with significant reductions in unnecessary exposure to broad-spectrum agents.

The IDSA, the Society for Healthcare Epidemiology of America, and the Centers for Disease Control and Prevention recommend syndrome-specific antimicrobial stewardship interventions as 1 strategy to reduce inappropriate antibiotic use.\(^34,35\) Other ASPs have implemented successful syndrome-specific initiatives targeting SSTIs. Jenkins et al\(^33\) found that an intervention that included dissemination of an institutional clinical practice guideline, development of an electronic order set, recruitment of physician champions, and quarterly feedback to physicians of adherence to the guideline to standardize and streamline the evaluation and treatment of inpatient uSSTIs led to shorter mean duration of therapy (13 days vs 10 days; \( P < .001 \)). In addition, fewer patients received antibiotics with broad gram-negative (66% vs 36%; \( P < .001 \)), anaerobic (76% vs 49%; \( P < .001 \)), and antipseudomonal (28% vs 18%; \( P = .02 \)) activity without adversely affecting clinical failures (7.7% vs 7.4%; \( P = .93 \)).\(^33\) Pasquale et al\(^36\) found that the addition of formal ASP guidance via prospective audit with feedback for SSTIs can reduce the

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**TABLE 2. Imaging and Blood Culture Use\(^{a,b}\)**

| Variable     | AGH Preintervention (n=117) | AGH Postintervention (n=100) | AGH P value | WPH Preintervention (n=43) | WPH Postintervention (n=63) | WPH P value | Total cohort Preintervention (n=160) | Total cohort Postintervention (n=163) | Total cohort P value |
|--------------|----------------------------|----------------------------|-------------|-----------------------------|-----------------------------|-------------|-------------------------------------|-------------------------------------|---------------------|
| Blood cultures | 95 (81.2)                  | 80 (80.0)                  | .86         | 30 (69.8)                   | 40 (63.5)                   | .54         | 125 (78.1)                         | 120 (73.6)                         | .37                 |
| CT           | 21 (18.0)                  | 14 (14.0)                  | .46         | 6 (14.0)                    | 8 (12.7)                    | .99         | 27 (16.9)                          | 22 (13.5)                          | .44                 |
| MRI          | 5 (4.3)                    | 2 (2.0)                    | .46         | 8 (18.6)                    | 6 (9.5)                     | .24         | 13 (8.1)                           | 8 (4.9)                            | .27                 |
| Radiography  | 65 (55.6)                  | 51 (51.0)                  | .59         | 25 (58.1)                   | 30 (47.6)                   | .33         | 90 (56.3)                          | 81 (49.7)                          | .27                 |

\(^{a}\)AGH = Allegheny General Hospital; CT = computed tomography; MRI = magnetic resonance imaging; WPH = Western Pennsylvania Hospital.

\(^{b}\)Data are presented as No. (percentage).
inpatient length of stay compared with historical data (6.2 days vs 4.4 days; \( P < .001 \)). We believe that these studies highlight that there is not only 1 correct tactic when implementing a syndrome-specific initiative and that the interventions should be tailored to the needs of the individual institution coupled with the resources available. In comparison with the SSTI interventions performed by Jenkins et al, our ASP-bundled approach likely required greater ASP resources given the dedicated personnel time necessary to perform daily prospective audits with real-time intervention and feedback. However, our bundled approach was associated with 79%, 75%, and 89% relative reductions in the use of antibiotics with extended gram-negative, extended anaerobic, and antipseudomonal coverage in patients with uSSTIs, respectively, whereas the approach used by Jenkins et al, which did not use prospective audit with real-time intervention, was associated with 45%, 36%, and 36% relative reductions, respectively.

Our current evaluation has several important limitations. First, it was a retrospective analysis in which case finding was reliant on ICD-9 and ICD-10 coding from hospital discharge data, and this strategy may have led to underestimation of the true number of hospitalized patients with uSSTIs at our institutions. Second, the retrospective nature of our study design allowed for reviewer bias. Despite chart reviewers not being blinded, we attempted to limit the potential for reviewer bias by using objective end points as well as electronic data extraction for capture when possible. Third, the retrospective nature of our preintervention and postintervention evaluation lends itself to the potential for period bias. However, there were no other initiatives or ASP processes implemented during this time period aimed at altering hospital antibiotic prescribing practices for uSSTIs. Also, as all portions of the bundle were implemented simultaneously, it is not possible to tease out the effect of each individual component and we are only able to determine the effect of the bundle as a whole rather than the contributions of each part of the bundle. In addition, postdischarge statistical analyses were limited to readmissions to AGH and WPH. Visits to other inpatient facilities, urgent care centers, and physicians’ outpatient offices may have been missed, leading to an inability to determine rates of treatment failure or the need to extend or reintroduce antibiotic therapy. We were also unable to assess adherence to outpatient antibiotics. As our inclusion criteria were intentionally selected to include only those patients with uSSTIs, we cannot comment on

### TABLE 3. Antibiotic Treatment Duration\(^{a,b}\)

| Variable                  | AGH       | WPH       | Total cohort |
|---------------------------|-----------|-----------|--------------|
|                           | Preintervention | Postintervention | Preintervention | Postintervention | Preintervention | Postintervention | Preintervention | Postintervention |
| Total antibiotic duration (d) | 12.6±3.5  | 9.1±2.3   | 12.5±3.8     | 8.8±2.2     | 9.1±2.3         | 8.4±2.0         | 8.4±2.0         | 8.8±2.2     |
| Appropriate duration (d)   | <.001     | <.001     | <.001        | <.001       | <.001           | <.001           | <.001           | <.001       |
| Total antibiotic duration (d) | <.001     | <.001     | <.001        | <.001       | <.001           | <.001           | <.001           | <.001       |
| Inappropriate duration (d) | 22 (18.8) | 63 (63.0) | 11 (25.6)    | 49 (77.8)   | 33 (20.6)       | 112 (68.7)      | 33 (20.6)       | 112 (68.7)  |
| Gram-negative coverage     | 62 (53.0) | 36 (36.0) | 21 (48.8)    | 14 (22.2)   | 83 (51.9)       | 50 (30.7)       | 83 (51.9)       | 50 (30.7)   |
| Anaerobic coverage         | 44 (37.6) | 12 (12.0) | 19 (44.2)    | 4 (6.3)     | 63 (39.4)       | 16 (9.8)        | 63 (39.4)       | 16 (9.8)    |
| Antipseudomonal coverage   | 19 (16.2) | 3 (3.0)   | 16 (39.5)    | 1 (1.6)     | 26 (16.3)       | 3 (1.8)         | 26 (16.3)       | 3 (1.8)     |

\(^{a}\)AGH = Allegheny General Hospital; WPH = Western Pennsylvania Hospital.

\(^{b}\)Data are presented as mean ± SD or as No. (percentage).

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those patients with SSTIs with complicating factors and the ability of an ASP-bundled intervention to affect optimal antibiotic prescribing in this subset of patients. Further study is needed in patients with SSTIs and additional complicating factors.

Our evaluation has numerous strengths. Our study focused on 2 centers with different patient populations and medical care providers. The results were similar between the facilities with significant reductions in both durations of therapy and unnecessary use of agents with extended gram-negative and anaerobic coverage. Our ASP-bundled intervention was able to positively affect antibiotic prescribing practices at both institutions, suggesting that the intervention itself is applicable across different types of hospitals. Also, in the postintervention period, we included all patients with a primary ICD-9 or ICD-10 code for SSTI who met prespecified study criteria, regardless of whether they were able to be evaluated by the ASP team. This allowed us to better determine the effect of the bundled intervention rather than focusing on the effect of ASP audit with feedback alone.

Strategies to reduce the use of our limited armamentarium of antimicrobial agents are greatly needed in the era of the rise in antimicrobial resistance. Given their significant effect on morbidity and mortality, multidrug-resistant bacteria are considered one of the largest threats to public health by numerous prominent organizations including the Institute of Medicine, the Centers for Disease Control and Prevention Task Force on Antimicrobial Resistance, and the IDSA.21-24 Our study suggests that the implementation of a syndrome-specific intervention via use of an ASP-bundled approach represents a practical tactic to dramatically reduce antimicrobial use by reducing the duration of therapy and promoting narrow-spectrum therapy. Given that our initiative exemplifies an efficacious syndrome-specific strategy for a commonly encountered infection, it is critical to analyze the effectiveness of this bundled approach, using intensive education, multidisciplinary creation of a clinical decision-making algorithm, and prospective audit with real-time intervention, for other common infections in hospitalized patients.

CONCLUSION
Implementation of an ASP-bundled approach aimed at optimizing antibiotic therapy in the management of uSSTIs led to shorter durations of narrow-spectrum therapy and shorter hospital length of stay without adversely affecting hospital readmissions.

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SUPPLEMENTAL ONLINE MATERIAL
Supplemental material can be found online at: http://www.mcpiqojournal.org. Supplemental material attached to journal articles has not been edited, and the authors take responsibility for the accuracy of all data.

Abbreviations and Acronyms: AGH = Allegheny General Hospital; ASP = antimicrobial stewardship program ICD-9 = International Classification of Diseases, Ninth Revision; ICD-10 = International Classification of Diseases, Tenth Revision; IDSA = Infectious Diseases Society of America; SSTI = skin and soft tissue infection; uSSTI = uncomplicated skin and skin tissue infection; WPH = Western Pennsylvania Hospital

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ANTIMICROBIAL STEWARDSHIP EFFECT ON CELLULITIS

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