Clinical Review

ACUTE BACTERIAL SKIN AND SKIN STRUCTURE INFECTIONS (ABSSSI): PRACTICE GUIDELINES FOR MANAGEMENT AND CARE TRANSITIONS IN THE EMERGENCY DEPARTMENT AND HOSPITAL

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Abstract—Background: Acute bacterial skin and skin structure infections (ABSSSI), formally referred to as complicated skin and soft tissue infections, include infections with resistance to previously effective antimicrobials. Increasing dramatically in incidence, they have become a challenging medical problem associated with high direct and indirect costs to both the medical system and society. Objectives: To describe the burden of ABSSSI and to explore multidisciplinary approaches to its management and new treatments that can be initiated in the emergency department. Discussion: We offer a best practice model aimed at providing risk-stratified and convenient care for ABSSSI at the lowest possible cost, while minimizing complications, readmissions, and inappropriate antibiotic use. In doing so, we focus on the care provided by emergency physicians and hospitalists and the transition of management between them for inpatient care, as well as the facilitation of observation or direct-to-outpatient care for suitable patients. Conclusions: A standard, consistent, and multidisciplinary approach to ABSSSI can streamline care, reduce admissions, support antimicrobial stewardship, and improve clinical and resource consumption outcomes. © 2015 Elsevier Inc.

Keywords—skin infections; ABSSSI; processes of care; best practice; antibiotics

INTRODUCTION

Acute bacterial skin and skin structure infections (ABSSSI) have become a challenging medical problem associated with high direct and indirect costs to both the medical system and society. Infections due to bacteria with resistance to previously effective antimicrobials such as methicillin-resistant Staphylococcus aureus (MRSA) are increasing in incidence and have led to higher rates of complications and hospitalization. MRSA has emerged as the most common cause of purulent infections in the United States and many other areas. Meeting the challenge to deliver efficient health care not
only demands that we recognize and treat individual patients; we must also define strategies to optimize patient flow and resource utilization. An important goal is to limit inpatient stays and reduce hospital readmissions through seamless transitions of care from the emergency department (ED) into the hospital medicine service, and then out to the community. The purpose of this report is to describe a best practice model for patient care and resource management in ABSSSI.

**Why ABSSSI and not cSSTI?**

The terms “skin and skin structure infection” and “skin and soft tissue infection” (SSTI) were coined to describe infectious processes such as cellulitis, erysipelas, cutaneous abscesses, and infected wounds, ulcers, or burns. The designation of more severe SSTI included a lower-case “c” (cSSTI) for “complicated” skin and soft tissue infection and typically implied a need for inpatient management, surgical procedures, or a significant underlying comorbidity such as diabetes or systemic immunosuppression that complicates response to therapy.

In 2013, to identify more clearly a severe subset of SSTI that would typically be treated with parenteral antibacterial therapy, the United States (US) Food and Drug Administration (FDA) issued guidance that standardized the nomenclature to be used in the evaluation of new antimicrobial treatments for cSSTI, which are now referred to as acute bacterial skin and skin structure infections, or ABSSSIs. The rationale for developing this terminology was to provide a consistent means of identifying infections for which a reliable drug treatment effect can be estimated. The agents to be studied under the new definitions are most often administered parenterally, and patient level of illness is reflected in parameters such as lesion size, leukocytosis, fever, and systemic inflammatory response syndrome (1).

The specific verbiage from the FDA is as follows:

ABSSSIs include cellulitis/erysipelas, wound infection, and major cutaneous abscess with a minimum lesion surface area of 75 cm². Diabetic foot ulcers and burn wound infections are excluded. Bacterial pathogens that commonly cause ABSSSI include *Streptococcus pyogenes* and *Staphylococcus aureus*, including MRSA strains. Less commonly identified bacteria include other *Streptococcus* species, *Enterococcus faecalis*, and Gram-negative bacteria (1).

Although various terms appear in the literature and some of the studies discussed in this review used the terms cSSSI or cSSTI, we will use ABSSSI consistently to describe these complicated infections, to avoid confusion. The primary etiologic organism of concern in ABSSSI is MRSA, and most novel antimicrobials studied to date under the new FDA guidance target MRSA specifically.

**DISCUSSION**

**Management of ABSSSI: Time for a New Focus**

Skin and skin structure infections are common causes for presentation to the ED. The majority of these patients can be treated effectively as outpatients with oral antimicrobial agents, with or without minor surgical intervention. For patients with the more serious ABSSSI, who are deemed to require parenteral therapy, effective communication and care transition between the ED and the hospital medicine service are particularly important. A clearly defined methodology for evaluating the need for inpatient care and subsequent outpatient and inpatient management is currently absent. The objective of such a methodology should be to provide highest quality care. Secondarily, the goal is to give appropriate and convenient care at the lowest possible cost, while minimizing complications, readmissions, and inappropriate antibiotic use. We will first discuss why ABSSSIs are a high-priority infection that deserve immediate attention, and then describe why a consistent, quality-driven program to manage these patients is necessary.

**Why ABSSSI and MRSA are High-priority Infections**

- MRSA is prevalent in ABSSSI.
- Rates of MRSA infection and hospitalizations are dramatically increasing.
- MRSA and ASSSI have high rates of morbidity and other associated medical conditions.
- MRSA infection is a risk factor for subsequent hospitalization and death.
- Inadequate treatment of MRSA ABSSSI due to antibiotic resistance is likely a factor in relapse.
- Urgent need exists to reduce hospitalization through the use of more effective outpatient treatment strategies.
- Effective outpatient management can reduce cost and improve patient outcomes and satisfaction.

**Profile of ABSSSI Today: The Importance of MRSA**

Patients with ABSSSI present to EDs with a broad range of disease severity, ranging from cellulitis to serious, life-threatening, necrotizing infections. These infections may arise as the result of minor injuries that break the skin, from animal bites, to gunshot and knife wounds; or with no clear precipitating event.

As suggested by the FDA guidance above, staphylococci, predominantly MRSA, and to a lesser extent, methicillin-susceptible *S. aureus*, cause most skin infections. Some infections, such as those associated with a diabetic foot ulcer, are additionally caused by aerobic...
Gram-negative and anaerobic bacteria, and others, such as dog and cat bites, are due to specific zoonotic pathogens, such as *Pasteurella* spp. The etiology of cellulitis without a wound or drainage is unclear due to lack of culturable material, but is thought to be predominantly due to *Streptococcal* species such as *S. pyogenes*. In most instances, ED clinicians begin empiric antibiotic therapy for infections prior to knowing the results of culture and susceptibility testing. Given that in many cases of ABSSSI there are no positive wound or blood cultures giving subsequent definitive guidance, it is all the more important that empiric coverage be guided by recognition of the most common pathogens, which are Gram-positive cocci. Gram-negative coverage is not empirically indicated in most cases of ABSSSI (2,3).

The choice of empiric antibiotics has not always been optimal. For example, in one study of ED practice in 2004, before MRSA was recognized as a frequent cause of ABSSSI, 59% of patients were found to have infection caused by MRSA. Only 57% of these patients were prescribed an empiric antibiotic to which the isolate demonstrated in vitro resistance (4).

The wide spectrum of illness caused by MRSA includes not only ABSSSIs, but also bacteremia and endocarditis, pneumonia, bone and joint infections, necrotizing fasciitis/myositis, central nervous system infections, and toxic shock and sepsis syndromes. The emergence of MRSA is, however, a truly recent phenomenon. Prior to 2000, MRSA was more commonly encountered in nosocomial infections than in community-onset infections. A study of cutaneous abscesses associated with intravenous drug use in the early 1990s showed no methicillin resistance among the *S. aureus* isolates (5). Then, between 2001 and 2005, the prevalence of MRSA infections among ABSSSI cases increased from 29% to 64% in a single Los Angeles ED (6). In a geographically diverse network of EDs in the United States collecting isolates in the early 2000s, MRSA was identified as the most common cause of ABSSSI (4). Similarly, data from the SENTRY Antimicrobial Surveillance Program that evaluated causes and types of SSTI from 1998 to 2004 revealed that *S. aureus* was present in 44.6% of isolates in North America, of which 35.9% were methicillin resistant (7). By 2008, empiric coverage for MRSA in the ED management of ABSSSI was common (8).

Compared with hospital-associated MRSA (HA-MRSA), community-acquired MRSA (CA-MRSA) tends to be more virulent and may carry genes that encode the Panton-Valentine leukocidin, as well as many other exotoxins that are associated with tissue necrosis and greater severity of disease (9–13). Although many strains have emerged globally, in the United States, USA300 is the most common CA-MRSA strain (6,8,9,14,15).

**Scope of the Problem: the ED Perspective**

According to the National Hospital Ambulatory Medical Care Survey, the number of ED visits for skin infections almost tripled from the late 1990s until 2005, and continues to increase at an alarming rate (Figure 1) (1).

Data published in 2009 showed that ABSSSI (though discussed using different terminology at that time) accounted for almost 870,000 hospital admissions in the United States in 2004. This represents an increase of almost 30% in the incidence of this diagnosis over a 4-year period (16). Other studies have reported a 50% increase in outpatient visits for skin and skin structure infections over an 8-year period (17). These increases in disease incidence have been attributed primarily to the epidemic spread of CA-MRSA (16–18). The fact that CA-MRSA is now common, even though colonization in the general population is low, suggests that CA-MRSA may colonize other body sites or have virulence characteristics that favor de novo colonization and infection in susceptible hosts (19). In addition, during much of the first decade of this century, insufficient attention was paid by empiric prescribers to the role of MRSA in ABSSSI, and it is likely that prescribing practices played a role in the substantially increased incidence of MRSA infections.

**Morbidity and Mortality**

Although HA-MRSA has been increasingly implicated in life-threatening and fatal nosocomial infections, the impact of CA-MRSA infections may be underestimated because hospital-based bacteriologic surveillance studies often do not capture data on infected patients who are not admitted. In light of this information gap, Delaney and colleagues conducted a large cohort study comprised of 1439 patients in general practices diagnosed with CA-MRSA in the UK between 2001 and 2004, and 14,090

![Figure 1. Annual visits to United States emergency departments for selected acute bacterial skin and skin structure infections.](image-url)
matching noninfected patients from the General Practice Research Database, to assess mortality associated with community-diagnosed CA-MRSA infections (20). Their principal finding was that patients who develop a CA-MRSA infection are at significantly greater risk of mortality during the year after diagnosis, compared with patients who did not contract it: 21.8% vs 5.0%, respectively, as shown in Figure 2 (20). The patients with CA-MRSA commonly had comorbidities, such as diabetes, that are also associated with poor outcomes, so a truly causative link between MRSA and 1-year mortality may not exist; nonetheless, CA-MRSA may serve as a marker for “sicker” patients.

The Delaney study also revealed some important clinical associations between CA-MRSA infections and comorbid conditions among patients in the general practice population. Figure 3 shows the prevalence of various comorbidities in CA-MRSA patients, as compared to the prevalence of those diseases in patients who did not have MRSA infections (20). Note that diabetes, cardiovascular disease and stroke, peripheral vascular disease, chronic obstructive pulmonary disease, renal failure, and cancer were all more common in patients with MRSA infections than in MRSA noninfected patients. In the same study, patients with a diagnosis of MRSA were more likely to die (events/100 patient-years) than those without MRSA (unadjusted hazard ratio [HR] 4.85; 95% confidence interval [CI] 4.25–5.54), as shown in Figure 4 (20).

The HR for death from any cause in patients with a diagnosis of CA-MRSA was 4.08 (95% CI 3.54–4.69) as compared to patients without CA-MRSA, after adjustment for age, gender, and the comorbid conditions. Patients with CA-MRSA were also at greater risk of hospitalization or death within 1 year after diagnosis, with an adjusted HR of 3.31 (95% CI 2.97–3.69), compared to patients without MRSA. Antibiotic treatment for any cause in the year prior to study entry exerted only a small effect on mortality after adjustment for other factors, with an adjusted HR of 1.30 (95% CI 1.14–1.49). Among CA-MRSA patients without comorbidities, the risk of mortality was comparable to that for all patients, with an adjusted HR of 4.86 (95% CI 4.10–5.77) (20). The results of this study suggest that CA-MRSA is at least a marker of poor outcomes and, particularly in patients with significant comorbidities, should prompt particular attention to hospital care and follow-up. A recent analysis of US Healthcare Cost and Utilization Project (HCUP) data by Talan found that the mortality rate of patients hospitalized for ABSSSI was 0.5% (21).

**Important Comorbidities with MRSA ABSSSI**

**Diabetes.** Data suggest that patients with types 1 and 2 diabetes are at 1.6 and 1.3 times greater risk of developing ABSSIs, respectively, compared with those without
diabetes (22). Given the increasing incidence of type 2 diabetes, this association may be in part responsible for increasing infection rates among the general population.

Suaya and colleagues investigated the relationship among diabetes, ABSSSIs, and complications of ABSSSIs in International Classification of Diseases, 9th Revision-stratified records of 140,652 patients with and 1,539,692 patients without diabetes, who were between the ages of birth and 64 years and had at least 1 episode of ABSSSI (22). The overall sample was comprised of 2,227,402 distinct episodes of ABSSSI, of which 10% occurred in patients with diabetes (22). Among patients with ABSSSIs whose initial diagnoses occurred in outpatient settings, the most commonly observed complication was osteomyelitis, which occurred in 3.3% of patients with, and 0.4% of patients without, diabetes ($p < 0.01$). Bacteremia, endocarditis, septicemia, and sepsis were the most commonly reported inpatient complications associated with ABSSSI, and occurred in 25% of patients with, and 16% of patients without, diabetes ($p < 0.01$). Rates of hospital admission were significantly higher among patients with, compared to those without, diabetes for all sites and types of ABSSSI, with the exception of folliculitis (22). These results suggest the need for more cautious evaluation and management of diabetic patients with ABSSSI, and closer follow-up, due to the potential for complications.

**Advanced age.** Data from HCUP reveal that the highest rate of MRSA hospitalization is among the elderly—360.8 MRSA stays per 100,000 patients over 65 years of age (23). This is more than three times higher than for any other age group: 114.7 stays for infants, 19.2 for 1- to 17-year-olds, 58.1 for 18- to 44-year-olds, and 111.5 for 45- to 64-year-olds per 100,000 (Figure 5) (23). This may reflect higher hospital exposure, a higher burden of comorbidities, diminished immune function, or some combination of these and other factors.

**ED as the “Portal of Entry”**

Inpatients with MRSA ABSSSI infections are more likely to be first cared for in the ED than to be transfers from another hospital, or to be transfers from long-term care settings (Figure 6) (23). Although it may not be surprising that the largest number of patients with MRSA infections were admitted from the ED, this finding underscores the importance of having a well-defined process for identifying, risk-stratifying, and empirically managing patients with ABSSSI both in the ED and all the way through their hospital course.

**Cost of Treatment**

Cost containment and cost-efficient patient management are top priorities today for hospitals, health systems, and Accountable Care Organizations. The estimated mean cost of an ABSSSI hospitalization in the United States is $8023 with a 4.9-day length of stay and associated risks. Lee and colleagues developed an economic simulation model to quantify CA-MRSA-associated (specifically; these figures may not be generalizable to all ABSSSI) costs from societal and third-party payer...
perspectives (24). They noted that hospitalization rates and mortality are important cost drivers and that CA-MRSA infections result in a substantial economic burden on third-party payers and society. Major contributors to the total societal economic burden include CA-MRSA-attributable productivity losses. Their findings were as follows (24):

- Cost of a single CA-MRSA case to a third-party payer: $2277–$3200
- Cost to society: $7070–$20,489, depending on patient age
- Annual burden to U.S. third-party payers: $478 million to $2.2 billion
- Annual burden to society (U.S.): $1.4–13.8 billion on society, depending on the CA-MRSA definitions and incidences

Results of an observational study that was conducted in a primary care setting built on the above findings showed that 1 in 5 patients with CA-MRSA who presents to a primary care setting is likely to require additional interventions, each of which is associated with a cost of almost $2000 per incident (25).

**Risk Stratification in the ED**

A major component of clinical decision-making in the ED involves risk stratification (26–29). This is certainly true of ABSSSI, for which life- or limb-threatening infection must be distinguished from less severe infections. We describe and recommend a step-wise approach to ABSSSI risk stratification.

**Assess for hemodynamic instability.** For patients with skin and skin structure infections who are hemodynamically unstable, resuscitation should begin immediately, accompanied by appropriate antimicrobial coverage. Necrotizing infections should be considered (see next). These patients are typically admitted to the hospital, often to intensive care settings. Hemodynamically stable but acutely ill patients with ABSSSI should be screened for sepsis as per institutional protocols/pathways (30).

**Assess for possible necrotizing fasciitis.** This is largely a clinical assessment, taking into account signs of severe sepsis, disproportionate pain, rapidity of advancement, and evidence of soft tissue gas, compartment syndrome, or muscle necrosis (e.g., elevated creatine phosphokinase). This evaluation can be enhanced by use of the Laboratory Risk Index for Necrotizing Fasciitis (LRINEC). This score was developed about 10 years ago on the basis of a study of 145 patients who were admitted with the diagnosis of necrotizing fasciitis, compared to a control population of 309 patients hospitalized for cellulitis or abscess (31). Abnormalities of the total white blood cell count (15–25,000/mm³ = 1 point; > 25,000 = 2 points), hemoglobin (11–13.5 g/dL = 1 point, < 11 g/dL = 2 points), sodium (<135 mEq/L = 2 points), glucose (>180 mg/dL = 1 point), serum creatinine (>1.6 mg/dL = 2 points), and C-reactive protein (>150 mg/L = 4 points) were used to construct a score by converting the regression coefficients of independently predictive factors for diagnosing necrotizing fasciitis. The cutoff value for the LRINEC score was ≥ 6 points, with a positive predictive value of 92.0% and negative predictive value of 96.0%. The score is one tool that can be used along with clinical judgment and serial observations (e.g., observing a drawn border of the lesion for progression) to determine if necrotizing ABSSSI is likely.

Necrotizing fasciitis is a clinical diagnosis for which emergency surgical exploration and treatment, if the diagnosis is confirmed, should not be delayed. Expedited computed tomography (CT) and magnetic resonance imaging (MRI), by showing better than plain radiography the extent and detail of deep tissue involvement, and gas when present, may have a role in stable patients in whom the diagnosis is uncertain. These advanced imaging findings, when present, however, are often nonspecific and thus, may further delay potentially critical surgery. It is important to note that findings of necrotizing fasciitis—subcutaneous thickening, air, and fascial fluid—have also been appreciated on bedside ultrasound, and use of this modality in the ED may save time (32,33).

**Evaluate for unstable comorbidities.** Comorbidities may have a significant impact on outcomes and mortality in ABSSSI and may independently require inpatient management. If the patient has diabetic ketoacidosis or has an acute exacerbation of any other disease that could jeopardize the success of outpatient treatment, hospital admission is indicated.

**Assess for high-risk locations and lesions that require extensive surgery.** Infections involving certain areas may require more careful evaluation and monitoring in the hospital, such as orbital cellulitis and hand infections. In larger and more indurated lesions in which there is a possibility of a deep abscess that cannot be discerned by clinical examination, soft tissue ultrasound may provide valuable information. Patients with large and deep abscesses, and infected areas that require extensive debridement, may require hospitalization for operative treatment and intensive physical therapy. Inadequate drainage is often a reason for apparent failure of an initial outpatient antibiotic regimen (34).

**Identify social and personal factors that would interfere with successful outpatient care.** The patient’s home and
emotional condition should be evaluated. Those with no social support and for whom such support cannot be found or arranged, or who are deemed to be psychologically unstable or unreliable with regard to following treatment instructions and meeting follow-up needs, may need inpatient treatment. Ongoing intravenous drug use may also be an important consideration, both as a portal of entry for ABSSSI and a concern for reliability regarding compliance.

Many patients who do not have these indications for hospitalization can be managed as outpatients with close follow-up and treated with various outpatient strategies. These strategies include oral antibiotics, a once-a-day parenteral antibiotic given in the ED with the peripheral catheter left for next-day follow-up and additional dosing, insertion of a peripheral intravenous central catheter (PICC) and outpatient parenteral antibiotic therapy (OPAT), and new extended half-life parenteral lipoglycopeptides for single-dose or weekly dose treatment (35–37).

Neither the presence nor magnitude of fever precludes outpatient management. For example, two randomized, double-blind, double-dummy trials comparing dalbavancin, two injections one week apart, to intravenous vancomycin for at least 3 days followed by oral linezolid, found similar response rates and no septic deaths among 1315 admitted ABSSSI patients with areas of erythema > 300 cm² and frequent fever (84% had temperature > 38.0°C). Overall, approximately 25% of the patients in these two trials received all treatment for their infections on an outpatient basis (34,36). The availability of oritavancin has the potential to increase the use of that option even further, as a second dose is not required (38).

**Choice of Antibiotics**

Considerations in selection of an empiric antibiotic for the treatment of ABSSSI in the ED include likely bacteriologic etiology, susceptibility, spectrum, host status (e.g., neutropenia, immunocompromise, diabetes), compliance, allergies, and location. Guidelines from the Infectious Diseases Society of America published in 2014 avoid recommending specific agents over one another (39). This reflects an evidence basis of clinical trials that were designed to be noninferiority comparisons. We therefore follow that approach, recognizing that emergency physicians and hospitalists frequently must make empiric treatment decisions that are complex for any individual patient.

Current recommendations for the treatment of skin infections when MRSA is suspected or identified are shown below (39). For each of the two disease categories, the recommended antibiotic and adult dose (in nonpregnant patients with normal hepatic and renal function) are provided:

- **Purulent cellulitis (defined as cellulitis associated with purulent drainage or exudate in the absence of a drainable abscess)**
  - Clindamycin, 300–450 mg orally (p.o.) 3 times daily
  - TMP-SMX (trimethoprim-sulfamethoxazole), 1–2 double strength tab p.o. twice daily
  - Doxycycline, 100 mg p.o. twice daily
  - Minocycline, 200 mg × 1, then 100 mg p.o. twice daily
  - Linezolid, 600 mg p.o. twice daily

- **Complicated SSTI (now called ABSSSI)**
  - Vancomycin, 15–20 mg/kg/dose intravenously (i.v.) every 8–12 hours (q8–12h)
  - Linezolid, 600 mg p.o./i.v. q12 h
  - Daptomycin, 4 mg/kg/dose i.v. q24 h
  - Telavancin, 10 mg/kg/dose i.v. q24 h
  - Clindamycin, 600 mg p.o./i.v. q8h
  - Tedizolid, 200 mg p.o./i.v. q24 h
  - Dalbavancin, 1000 mg i.v. on day 1, then 500 mg i.v. on day 8
  - Oritavancin, 1200 mg i.v. single dose

Some of the common considerations pertinent to emergency physicians and hospitalists with regard to the choice of FDA-approved parenteral antibiotics with MRSA activity for more serious ABSSSI are summarized in Table 1. These represent the opinions and clinical experience of the authors and are not official guidelines or recommendations. They are not meant to represent a complete list of all important considerations. They also serve as a reminder that understanding the perspectives of all members of the treatment team can help to create a smoother transition from the ED to the hospital and better coordination of care. In general, hospital-based providers should be attuned to identifying opportunities for improving antimicrobial stewardship, choosing drugs and doses that are safe and effective for the acutely ill patient, accounting for comorbidities such as impaired renal function that may impact dosing and monitoring regimens, and following culture and sensitivity results once available. “Antimicrobial stewardship” refers to coordinated interventions designed to improve and measure the appropriate use of antimicrobials by promoting the selection of the optimal antimicrobial drug regimen, dose, duration of therapy, and route of administration (40).

**Current Payment and Regulatory Forces Impacting the Management of ABSSSI**

Health care demands have forced hospitals and health systems to reevaluate care provided for many patient
populations. There are a number of factors that have led to the development of programs focused on different diseases. Table 2 outlines many of the factors that may lead emergency physicians and hospitalists to streamline and standardize management of ABSSSI (40–43).

As health care becomes increasingly regulated, medical practice becomes increasingly scrutinized. Not only are improved outcomes without complications expected, but in addition, care must be delivered in a manner that is streamlined, efficient, and without waste. It may be difficult for frontline physicians to keep up with the litany of mandates.

Evaluating ABSSSI as an example in this new and ever-changing care and reimbursement paradigm suggests how a systems-based and standardized management plan may be helpful. Programs should evaluate and limit

<table>
<thead>
<tr>
<th>Drug</th>
<th>Considerations for Emergency Physician</th>
<th>Considerations for Hospitalist</th>
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<tbody>
<tr>
<td>Vancomycin</td>
<td>• Empiric treatment for suspected MRSA infections, particularly purulent infections, and for patients with severe sepsis</td>
<td>• May not be indicated for pure cellulitis • Reevaluate empiric use after consideration of wound specimen rapid MRSA diagnostic test and culture and sensitivity results • Monitor for renal toxicity • Consider measuring MICs and vancomycin troughs to target higher levels for refractory infections</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>• Consider in patients with vancomycin allergy or risk of renal impairment • Allows i.v. to p.o. transition • Consider avoiding if patient has risk for <em>Clostridium difficile</em> infection • Consider local drug resistance patterns</td>
<td>• Adjunctive treatment in necrotizing fasciitis to reduce toxin production • Monitor for diarrhea and <em>Clostridium difficile</em> infection</td>
</tr>
<tr>
<td>Daptomycin</td>
<td>• Consider in patients with vancomycin allergy or risk of renal impairment</td>
<td>• High drug cost • Monitor for myopathy and rhabdomyolysis • Consider higher-than-standard dosing in severely ill patients</td>
</tr>
<tr>
<td>Ceftaroline (includes Gram-negative coverage)</td>
<td>• Consider in patients with vancomycin allergy or risk of renal impairment • Consider in suspected polymicrobial infections</td>
<td>• High drug cost • Evaluate need for broad spectrum coverage based on culture and susceptibility results</td>
</tr>
<tr>
<td>Linezolid</td>
<td>• Consider in patients with vancomycin allergy or risk of renal impairment • Allows i.v. to p.o. transition • Avoid in patients with low platelet counts and consider drug interactions</td>
<td>• Monitor blood counts, particularly platelets • High drug cost</td>
</tr>
<tr>
<td>Tigecycline (includes Gram-negative coverage)</td>
<td>• Consider in patients with vancomycin allergy or risk of renal impairment • Consider in polymicrobial infections • Boxed warning for increased all-cause mortality</td>
<td>• High drug cost • Evaluate need for broad spectrum coverage based on culture and susceptibility results • Boxed warning for increased all-cause mortality • Monitor for GI intolerances, hepatic dysfunction, and pancreatitis</td>
</tr>
<tr>
<td>Tedizolid</td>
<td>• Can be administered either orally or as an i.v. infusion • Once-daily dosage of 200 mg for 6 days</td>
<td>• High drug cost • Can be switched to i.v. infusion from oral if required • Patient can be switched from i.v. to oral at appropriate times • No boxed warning • Good tolerability profile</td>
</tr>
<tr>
<td>Dalbavancin</td>
<td>• Two doses, 1 week apart, may avert hospitalization • High drug cost balanced against savings from shorter or averted hospitalization</td>
<td>• Consider as alternative to PICC and OPAT, or incorporate into less intensive (fewer visits) OPAT regimen • Will require new coordination of care processes, largely driven by emergency physicians and hospitalists</td>
</tr>
<tr>
<td>Oritavancin</td>
<td>• One single i.v. dose may avert hospitalization • 3-h infusion time • May be well suited for patients at risk of loss to follow-up</td>
<td>• Consider as alternative to PICC and OPAT • Will require new coordination of care processes, largely driven by emergency physicians and hospitalists</td>
</tr>
</tbody>
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ABSSI = acute bacterial skin and skin structure infection; MRSA = methicillin-resistant *Staphylococcus aureus*; MIC = minimal inhibitory concentration; i.v. = intravenous; p.o. = per os (oral); GI = gastrointestinal; PICC = peripheral intravenous central catheter; OPAT = outpatient parenteral antibiotic therapy.
Choosing Wisely Campaign (43) Encourages the elimination of wasteful procedures and tests

Table 2. Factors That May Lead to Streamlining and Standardizing the Management of ABSSSI (Consensus of Authors)

<table>
<thead>
<tr>
<th>Health Care Mandate</th>
<th>Definition</th>
<th>ABSSSI Impact</th>
</tr>
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<tbody>
<tr>
<td>Affordable Care Act (Value based purchasing, ACOs)</td>
<td>Requires coordination across all treatment venues (outpatient, ED, and inpatient), as poor patient outcomes such as readmissions may not be reimbursed</td>
<td>Requires systems to evaluate hospital necessity critically, and develop programs to avoid denied payments. As ABSSSI is a condition that is common and may improve quickly, hospital programs standardizing evaluation and management may help treatment decisions</td>
</tr>
<tr>
<td>ED Throughput (CMS Core Measure) (41)</td>
<td>Requires EDs to establish benchmarks and improve patient flow. Success requires coordinated efforts between ED and hospitalists</td>
<td>Requires systems to evaluate hospital necessity critically, and develop programs to avoid denied payments. As ABSSSI is a condition that is common and may improve quickly, hospital programs standardizing evaluation and management may help treatment decisions</td>
</tr>
<tr>
<td>CMS Two Midnight Rule (42)</td>
<td>Changes benchmark for consideration of hospitalization vs observation such that inpatient services provided for an interval not reaching two midnights after admission may not be considered reimbursed for hospitalization. Requires coordinated efforts between ED and hospitalists, including optimal use of observation status</td>
<td>Requires systems to evaluate hospital necessity critically, and develop programs to avoid denied payments. As ABSSSI is a condition that is common and may improve quickly, hospital programs standardizing evaluation and management may help treatment decisions</td>
</tr>
<tr>
<td>Antimicrobial Stewardship (40)</td>
<td>Hospitals must improve utilization of antimicrobials. Impacts initial antimicrobial selection (ED) and follow-up therapy (hospitalist)</td>
<td>MRSA is a common cause of ABSSSI. Programs that encourage testing using rapid identification of resistant organisms (ED) and timely follow-up (hospitalist) may reduce overly-broad spectrum coverage and improve outcomes and cost standardized management of ABSSSI may avoid unnecessary testing</td>
</tr>
<tr>
<td>Choosing Wisely Campaign (43)</td>
<td>Encourages the elimination of wasteful procedures and tests</td>
<td>Standardized management of ABSSSI may avoid unnecessary testing</td>
</tr>
</tbody>
</table>

ABSSSI = acute bacterial skin and skin structure infection; ACO = Accountable Care Organization; ED = emergency department; CMS = Centers for Medicare & Medicaid Services; MRSA = methicillin-resistant Staphylococcus aureus.

the use of relatively low-yield diagnostic tests, such as erythrocyte sedimentation rate, for which there is no defined role in ABSSSI unless osteomyelitis is suspected. Use of ED ultrasound instead of CT scans in ABSSSI to evaluate for deep abscesses can save time and resources (Choosing Wisely) (43). Use of MRI should be reserved for situations in which the result will importantly impact management (2). Standard antimicrobial regimens for empiric therapy (based on local resistance patterns), standard approaches to bacteriologic testing, and uniform patient follow-up procedures increase consistency and quality of care (Affordable Care Act [ACA]). Finally, emergency physicians and hospitalists must remain current with the availability of new antimicrobial options (such as long-acting agents with activity against MRSA) and with local capabilities for home infusion services and close follow-up.

Multidisciplinary ABSSSI evaluation and management programs can potentially contribute to better outcomes and coordination of care from the ED to the hospital (in patients who require admission) and from the ED/hospital to the outpatient setting (ACA, Two-Midnight Rule). As the majority of ABSSSI patients have a low mortality rate, hospital avoidance should be a consideration for ABSSSI programs, particularly for patients who have been assessed for the potential of complications and bad outcomes in a standardized fashion. The use of OPAT programs and new extended half-life parenteral agents promote cost-effective care and improve ED throughput by allowing ED discharge (ACA, ED throughput). By avoiding admission, naturally, readmissions would be minimized (ACA). Additionally, not only do OPAT programs improve care transitions out of the ED, they may also improve transitions out of the hospital, ensuring patients who may not have an available primary care physician close follow-up for their infection (ACA).

Another consideration specific to ABSSSI care is a different perspective on drug acquisition cost, based on the settings in which the drugs are used. The inclusion of “cost” is relevant for all branded agents (all have higher acquisition cost compared to generics), but drug acquisition cost is only one cost component in overall total cost per episode of care. With longer-acting antimicrobial agents, there is a potential opportunity for broader “cost avoidance” through shortening or wholly averting inpatient admission, reducing ancillary care requirements, and reducing the use of PICC lines. Shifting to an outpatient or ED-only site of care can also trigger a different reimbursement formula, such as under Medicare, where drugs are separately reimbursed. This is in stark contrast to the inpatient, fixed payment by diagnosis-related group (44).

ABSSSI programs developed on epidemiologic evidence, incorporating evidenced-based recommendations, and considering total, overall costs have the potential to improve patient outcomes, satisfaction, value, and will address the changing health care paradigm.
CONCLUSIONS

Infectious agents such as MRSA are increasing in incidence and have led to higher rates of complications and hospitalization for ABSSSI. According to the National Hospital Ambulatory Medical Care Survey, the number of ED visits for skin infections almost tripled from the late 1990s until 2005, and continues to increase at an alarming rate. MRSA is prevalent in ABSSSI with high rates of morbidity and other associated medical conditions.

Patients who develop CA-MRSA are at significantly greater risk of mortality during the year after diagnosis compared with patients who did not contract it, 21.8% vs. 5.0%, respectively. Diabetes, cardiovascular disease and stroke, peripheral vascular disease, chronic obstructive pulmonary disease, renal failure, and cancer are all more common in patients with MRSA infections than in disease-free patients. The highest rate of MRSA hospitalization is among the elderly—360.8 MRSA stays per 100,000 patients over 65 years of age. This is more than three times higher than for any other age group.

Inadequate treatment of MRSA due to antibiotic resistance is a factor in relapse of ABSSSI. More effective outpatient treatment is needed to reduce hospitalization. These management strategies should include programs that evaluate and limit the use of relatively low-yield diagnostic tests. Use of ED ultrasound instead of CT scans in ABSSSI to evaluate for deep abscesses can save time and resources. Use of MRI should be reserved for situations in which the result will importantly impact management. Standard antimicrobial regimens for empiric therapy (based on local resistance patterns), standard approaches to bacteriologic testing, and uniform patient follow-up procedures increases consistency and quality of care. Finally, emergency physicians and hospitalists must remain current with the availability of new antimicrobial options (such as long-acting agents with activity against MRSA) and with local capabilities for home infusion services and close follow-up.

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REFERENCES


ARTICLE SUMMARY

1. Why is this topic important?
   Acute bacterial skin and skin structure infections (ABSSSIs) are increasingly prevalent and exert a tremendous clinical and economic burden on health care and society at large. Most ABSSSIs present to the emergency department (ED) for care, and a systematic and multidisciplinary approach to their evaluation and management can improve outcomes.

2. What does this review attempt to show?
   There are many factors (clinical, economic, and regulatory) impacting optimal ED and hospital care of ABSSSIs. By collaborating with hospitalists and other providers, processes of care can be streamlined and improved.

3. What are the key findings?
   Systematic risk stratification to determine optimal care and disposition from the ED can improve clinical care and ED throughput. Collaboration with other hospital-based specialists such as hospitalists, pharmacists, and infectious disease specialists can result in more prudent utilization of antimicrobial therapy and health care resources.

4. How is patient care impacted?
   Optimal management of ABSSSI beginning in the ED leads to provision of appropriate and convenient care at the lowest possible cost, while minimizing complications, readmissions, and inappropriate antimicrobial use.