## **Concise Communication**



# Rate of positive cultures necessitating definitive treatment in patients receiving empiric vancomycin therapy

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#### Abstract

Vancomycin is a commonly prescribed empiric antibiotic used when methicillin-resistant *Staphylococcus aureus* (MRSA) infection is suspected. In this study, we aimed to determine the rate of culture-positive infection requiring vancomycin therapy.

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Vancomycin is commonly used when methicillin-resistant *Staphylococcus aureus* (MRSA) infections are suspected. Despite the almost ubiquitous use of vancomycin in healthcare institutions, some data indicate that the prevalence of invasive MRSA infections are decreasing.<sup>1</sup> Despite declining rates of MRSA infection, vancomycin has been reported to be the most prevalent antimicrobial agent used in the inpatient setting.<sup>2</sup> Due to its widespread use, data on the prevalence of infections requiring vancomycin for definitive therapy are needed.

Vancomycin is often continued unnecessarily, despite the lack of positive cultures. In one report, nearly 25% of vancomycin use was continued inappropriately, despite a lack of culture data suggesting that patients did not have an organism that would necessitate definitive therapy with vancomycin.<sup>3</sup> Although multiple studies have been conducted to evaluate inappropriate vancomycin use, few data are available to indicate the proportion of patients who receive vancomycin that need vancomycin is the most common parenteral drug used to treat infections in the inpatient setting, its use may not be warranted in most cases.<sup>2</sup> The purpose of the current study was to determine the rate of culturepositive MRSA infection or other organism requiring vancomycin therapy compared with overall vancomycin use.

#### **Methods**

This retrospective, observational study was conducted within Intermountain Healthcare. All patients receiving empiric intravenous (IV) vancomycin between January 1, 2014, and March 31, 2014, were evaluated to determine the rate of positive cultures necessitating

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continued vancomycin therapy. Patients were excluded if they received oral vancomycin, if they were <18 years of age, or if they were admitted to the pediatric or orthopedic specialty hospitals within the health system. Patient-specific microbiologic results were evaluated via chart review to determine whether the isolated bacteria would warrant continued therapy with vancomycin. The primary outcome variable was the rate of positive cultures that would necessitate definitive vancomycin therapy. Conditions or isolated bacteria that were considered appropriate for continued vancomycin therapy included MRSA infection, infection with other bacteria for which vancomycin would be considered the drug of choice, and drug allergy for which vancomycin was a second-line option. The Institutional Review Board of Intermountain Healthcare approved this study and granted a waiver of informed consent. The total number of patients requiring vancomycin was calculated as the percentage of the total number of patients who received vancomycin.

### Results

A total of 1,662 patients met the inclusion criteria and were evaluated to determine whether definitive therapy with vancomycin was warranted. Of the patients who received vancomycin, 186 (11.2%) had a positive culture for an organism that would make vancomycin appropriate as definitive therapy. Among all patients who received vancomycin, 140 (8.4%) had positive MRSA cultures.

The most common sources of infection in culture-positive patients were skin and soft-tissue infection (SSTI, 38%), followed by bacteremia (29%), and respiratory infection (19%). Other sources of culture positivity indicative of infection included bone and/or joint infections (7%), urinary tract infections (3.5%), and miscellaneous or other infections (3.5%).

#### Discussion

Vancomycin continues to be the most commonly used empiric antibiotic in the inpatient setting for suspected infections. Much of this use occurs in patients in whom MRSA is a suspected pathogen. However, the results of this study suggest that MRSA is a pathogen in only a small number of cases compared to the number of total cases in which vancomycin is used as an empiric agent. These results are supported by other studies showing that MRSA is not a prevalent pathogen for infections for which vancomycin is often used. For example, Self et al<sup>4</sup> found that only 0.7% of patients admitted for community-acquired pneumonia had confirmed MRSA, even though vancomycin or linezolid was administered to almost 30% of these patients. In addition, the most common indication for vancomycin use, as confirmed by the results of this study, is SSTI. Most nonpurulent cellulitis is thought to be caused by  $\beta$ -hemolytic streptococci.<sup>5,6</sup> Guidelines published by the Infectious Diseases Society of America recommend agents with activity against MRSA for SSTIs if there is cellulitis associated with "penetrating trauma, evidence of MRSA infection elsewhere, nasal colonization with MRSA, injection drug use, purulent drainage, or SIRS".6

Empiric therapy for suspected MRSA infection should be guided by geographic location. Rates of MRSA infection are different in different areas of the United States. For example, Moran et al<sup>7</sup> found that rates of MRSA in patients with SSTI presenting to the emergency department are higher in the southern region and lower in the northeastern and central parts of the United States. Considering these data, clinicians should use their best judgment in determining whether vancomycin would be an appropriate empiric therapy. All cultures in the Moran et al study that were positive for MRSA were from purulent wounds or abscesses and cellulitis with purulent exudate. This finding supports the argument that cellulitis or wounds with purulence should include antibiotic therapy with activity against MRSA.<sup>7</sup>

The results of this study suggest that vancomycin is overutilized to treat empiric infections and that MRSA infection is relatively rare compared to the frequency with which vancomycin is prescribed. Based on the results of this study, providers in some areas should expect to discontinue vancomycin therapy in up to 90% of patients for whom cultures are negative at 48 hours after initiation of vancomycin therapy.

Many data have been published regarding the early attainment of therapeutic vancomycin serum concentrations, which the most appropriate way to obtain therapeutic trough concentrations, to obtain appropriate pharmacodynamic and pharmacokinetic parameters by which to monitor vancomycin therapy, and to ensure that nephrotoxicity is minimized.<sup>8,9</sup> Perhaps, however, there should be a shift in the research to determine how to most efficiently utilize stewardship efforts to ensure that vancomycin therapy is stopped when it is not indicated. Antimicrobial stewardship efforts regarding vancomycin should continue and should not only focus on pharmacodynamic or pharmacokinetic monitoring but also should encourage providers to discontinue vancomycin therapy when culture data or clinical presentation suggest that an MRSA infection is unlikely.

Our study has several limitations. First, this was only an observational study conducted in a geographically limited area.

Also, rates of MRSA may differ throughout the United States (and world); therefore, rates of MRSA in this study may not reflect rates of MRSA in other geographic locations. Second, lack of culture data for conditions such as cellulitis may have skewed the data for culture positivity and the use of antibiotics in this patient population. As previously mentioned, SSTIs were the most common source of culture positivity and were likely the most common indication for use of vancomycin, although indication was not directly assessed in the current study. Another limitation is that the definition of "appropriate" use of vancomycin is somewhat arbitrary, even in the case of negative cultures. Some patients may not have had abscesses drained for culture or may have had cultures performed elsewhere, and culture data may not have been available. Also, some use of vancomycin beyond 48 hours may have been due to failure of other antibiotic therapy for which culture data were not available.

In conclusion, vancomycin continues to be the most commonly used antibiotic to empirically treat infections in the inpatient setting. The results of the current study show that vancomycin continues to be used often in many cases in which the risk for MRSA (or other infection necessitating vancomycin therapy) is low.

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