Incorporating Point-of-Care Bacterial Fluorescence into a Wound Clinic Antimicrobial Stewardship Program

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Abstract

Background: In 2014 the World Health Organization (WHO) warned of an emerging world-wide crisis of antibiotic resistant microorganisms. In response, government and professional organizations recommended that health care systems adopt antimicrobial stewardship programs (ASPs). In the United States, the Centers for Medicare Services (CMS) mandated antimicrobial stewardship in the hospital inpatient setting. Effective January 1, 2020, the Joint Commission required ambulatory centers that prescribe antibiotics, such as wound centers, to institute an ASP.

Chronic wounds often remain open for months, during which time patients may receive multiple courses of antibiotics and numerous antimicrobial topical treatments. The wound clinician plays an integral role in reducing antimicrobial resistance in the outpatient setting: antibiotics prescribed for skin and soft tissue infections are among the most common in an outpatient setting. One of the most challenging aspects of antimicrobial stewardship in treating chronic wounds is the inaccuracy of bacterial and infection diagnosis.

Methods: Joint Commission lists five elements of performance (EP): (1) Identifying an antimicrobial stewardship leader, (2) establishing an annual antimicrobial stewardship goal, (3) implementing evidence-based practice guidelines related to the antimicrobial stewardship goal, (4) providing clinical staff with educational resources related to the antimicrobial stewardship goal,

and (5) collecting, analyzing, and reporting data related to the antimicrobial stewardship goal. This article focuses on choosing and implementing an evidence-based ASP goal for 2020.

Discussion: Clinical trials have demonstrated the ability of fluorescence imaging (MLiX) to detect clinically significant levels of bacteria in chronic wounds. Combined with clinical examination of signs and symptoms of infection, the MLiX procedure improves the clinician's ability to diagnose infection and can guide antimicrobial use. In order to satisfy the elements of performance, the MLiX procedure was incorporated into the annual ASP goal for several wound care centers. Clinicians were educated on the fluorescence imaging device and guidelines were instituted. Collection of antimicrobial utilization data is underway.

Keywords: antimicrobial stewardship, chronic wounds, clinical decision support, diagnostic pathway, fluorescence imaging, wound clinic

Introduction

The world-wide emergence of antibiotic resistant bacteria endangers the efficacy of antibiotics and increases the morbidity and mortality associated with infectious diseases.[1-3] In 2013, the Centers for Disease Control and Prevention (CDC) declared that mankind had entered a "post-antibiotic era.[4]" Shortly thereafter, the World Health Organization (WHO) warned of a dire antibiotic resistance crisis[5]. Although antimicrobial resistance may occur naturally over time, the misuse and overuse of antimicrobials has accelerated the process[5]. Antimicrobial stewardship plays a pivotal role in controlling bacterial resistance to antibiotics. Antimicrobial stewardship programs (ASPs), mandated in acute care settings and skilled nursing facilities, have successfully reduced antimicrobial use without sacrificing clinical outcomes[6]. This year hospital outpatient departments must institute ASPs[7].

The outpatient wound care center features prominently in the development of antimicrobial resistance for several reasons: antibiotic prescriptions written in the outpatient setting are most commonly for skin and soft tissue infections; the typical wound is open for more than three months during which time the patient may receive repeated courses of antibiotics and topical antimicrobials; and uninfected wounds with excessive inflammation are often misdiagnosed and treated as infected[8,9]. More importantly, the clinical signs and symptoms of infection are inaccurate and unreliable in chronic wounds[10]. Current diagnostic techniques, such as swabs, are fraught with

inaccuracies with regards to chronic wounds, and culture reports take days to return to the clinician[11]. In addition, they do not distinguish bacteria present in biofilms from planktonic forms and may not detect anaerobic bacteria or other potential pathogens that are, using standard hospital laboratory techniques, difficult to grow [12]. Quantitative tissue biopsies of the wound bed are more accurate than swabs but require an invasive procedure and it takes days for the results to return[12].

The MolecuLight procedure (MLiX) detects bacterial fluorescence in real time at the point-of-care[13,14]. The portable non-contact fluorescence imaging device emits violet light at 405nm that, under darkened room conditions, causes porphyrin-producing bacteria (e.g. *S. aureus)* to fluoresce red while *Pseudomonas aeruginosa* uniquely fluorescence cyan and tissue fluoresces green[15]. Under the violet light, red fluorescence is observed from most common wound pathogens (gram positive, gram negative, aerobes and anaerobes), including bacteria found in biofilm, though the red fluorescent signal cannot distinguish between biofilm and planktonic bacteria[16]. Prospective clinical trials have established the accuracy of this fluorescence imaging technology to identify the presence of moderate-to-heavy bacterial load with a positive predictive value of >95%[17,18] .   In wounds moderate bacterial load is defined as greater than 10^4 DFU. There is a robust body of evidence suggesting that bacterial loads at this level or greater inhibit wound healing[19]. Studies have reported high sensitivity and specificity of MLiX in detecting bacterial fluorescence in a variety of wounds including diabetic foot ulcers, venous leg ulcers, pressure ulcers, burns and surgical and trauma wounds[13,14,18-22]. Information provided by fluorescence imaging on the presence and location of bacteria at loads $>10^4$ CFU/g is used to target cleaning, debridement, and appropriate deployment of antimicrobials[14,18].

Effective January 1, 2020, the Joint Commission requires ambulatory centers, such as wound centers, that prescribe antibiotics to institute an ASP[7]. The Joint Commission lists 5 elements of performance to achieve this goal. This manuscript outlines how point-of-care fluorescence imaging to detect bacterial burden provides a potential solution that will satisfy the performance elements and comply with the ASP mandate.

Methods: Joint Commission lists five elements of performance (EP) on its website:

(1) Identifying an antimicrobial stewardship leader,

(2) Establishing an annual antimicrobial stewardship goal,

(3) Implementing evidence-based practice guidelines related to the antimicrobial stewardship goal,

(4) Providing clinical staff with educational resources related to the antimicrobial stewardship goal,

 (5) Collecting, analyzing, and reporting data related to the antimicrobial stewardship goal.

This manuscript proposes an evidenced-based solution to satisfy the five elements of performance (EP) and meet the requirements for an antimicrobial stewardship program (ASP) in the outpatient wound clinic. In 2020 SerenaGroup® advanced wound and hyperbaric centers instituted this ASP in all of its centers.

The clearest choice to satisfy EP-1, identifying an antimicrobial stewardship leader, is the medical director of the wound care center. Medical directors use their dedicated nonclinical time to direct the program, education staff and assist in data collection.

Today, the clinician relies on clinical signs and symptoms (CSS) in treating bacterial burden in chronic wounds; however, an increasing body of evidence suggests that CSS are unreliable. As a result, controlling antimicrobial use in the outpatient wound care center is problematic. To address this issue, the lead author established a 2020 antimicrobial goal (EP-2) of improving the detection of bacteria in chronic wounds.

Incorporation of the MLiX procedure into the assessment of chronic wounds fulfills the annual stewardship goal listed under EP-3. Identifying and treating elevated bacterial levels prior to the development of overt signs of infection, is expected to reduce the number of antibiotic prescriptions written, guide the use of topical antimicrobials, improve wound hygiene and direct debridement procedures. A robust body of evidence supports the integration of the MLiX into the ASP plan[13,14,17-22].

To satisfy EP-4, training and competencies on the MLiX procedure are available both in-person as part of the Challenges in Wound Care course series and online. A post-course test score of 80% and above is required for certification on image interpretation. Image interpretation is proctored by clinicians experienced with the device. Finally, data is collected at the site level from the

electronic health record and forwarded to a central research group for analysis and reporting fulfilling.

Discussion:

Presently, the prescription of topical antimicrobials and antibiotics in the wound clinic is best described as indiscriminate. This is not the fault of the woundologist. The assessment of clinical signs and symptoms of increased bacterial load are not sensitive enough on their own to identify levels of bacteria that may impede wound healing[14,18]. Standard laboratory swab cultures are inaccurate and do not permit real time prescribing[11]. The Joint Commission requires outpatient departments that prescribe antibiotics to institute antimicrobial stewardship programs (ASPs). The inability to accurately diagnose elevated bacterial burden in chronic wounds makes establishing an ASP problematic. ASPs have been proposed for wound centers, with rapid, point-of-care bacterial infection diagnostics highlighted as one potential solution[23]. We concur that a reliable ASP with reproducible data would benefit greatly from the incorporation of a point-of-care diagnostic for infection.

In a large multicenter clinical trial investigator changed their antimicrobial treatment 42% of the time based on the fluorescence image (figure1)[18]. In some cases, debridement removed bacteria resulting in the absence of fluorescence on the post-debridement image (figure 2). This was not true for all wounds that were debrided. It has also become clear that the use of the MLiX procedure as part of wound bed preparation could potentially reduce infectious complications associated with the application of Cellular or Tissue-based Products (Figure 3).
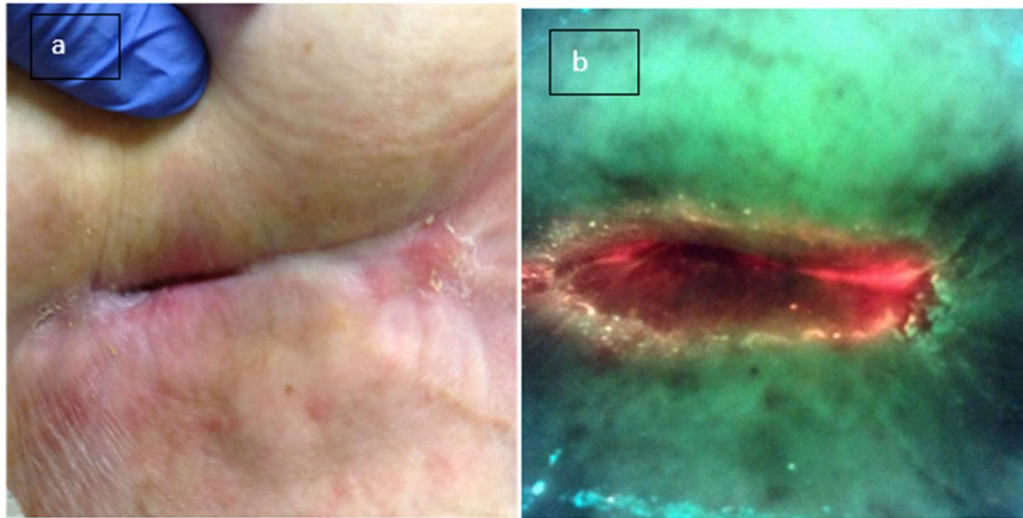
Figure 1: (a) Long-standing pressure ulcer negative for CSS. The physician planned to debride the wound and cover it with a foam dressing. (b) After viewing the red fluorescence she changed the plan: cleansing with hypochlorous acid and applying a topical antimicrobial. Biopsy confirmed $>10^5$ CFU/g
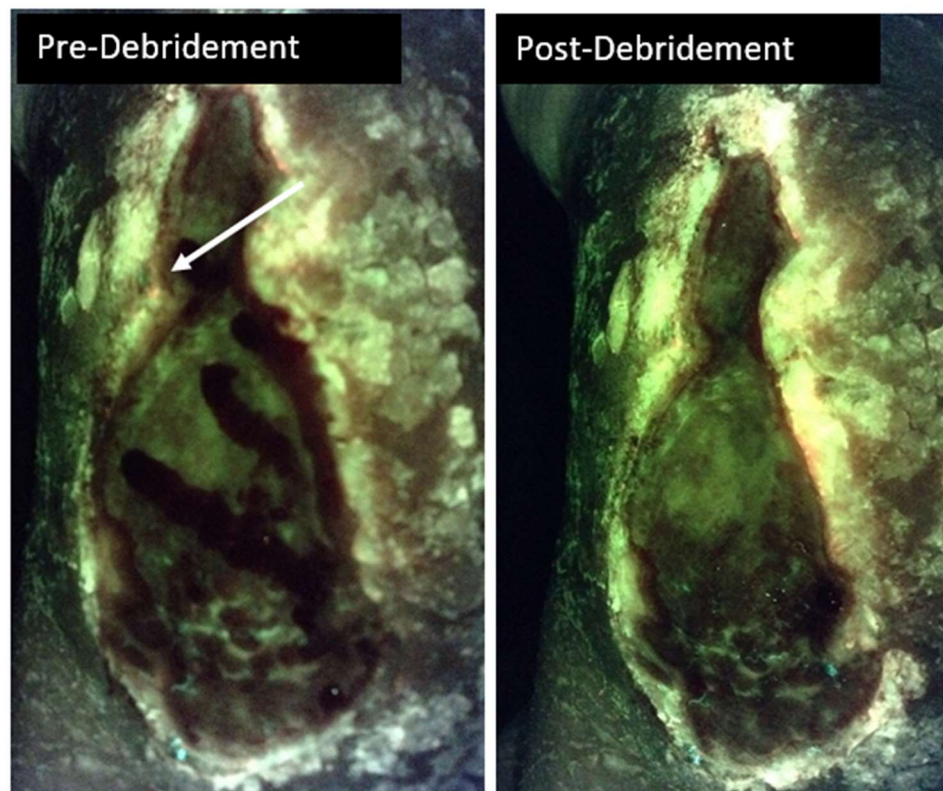

Figure 2: Fluorescence image pre and post debridement demonstrating the absence of fluorescence following debridement.
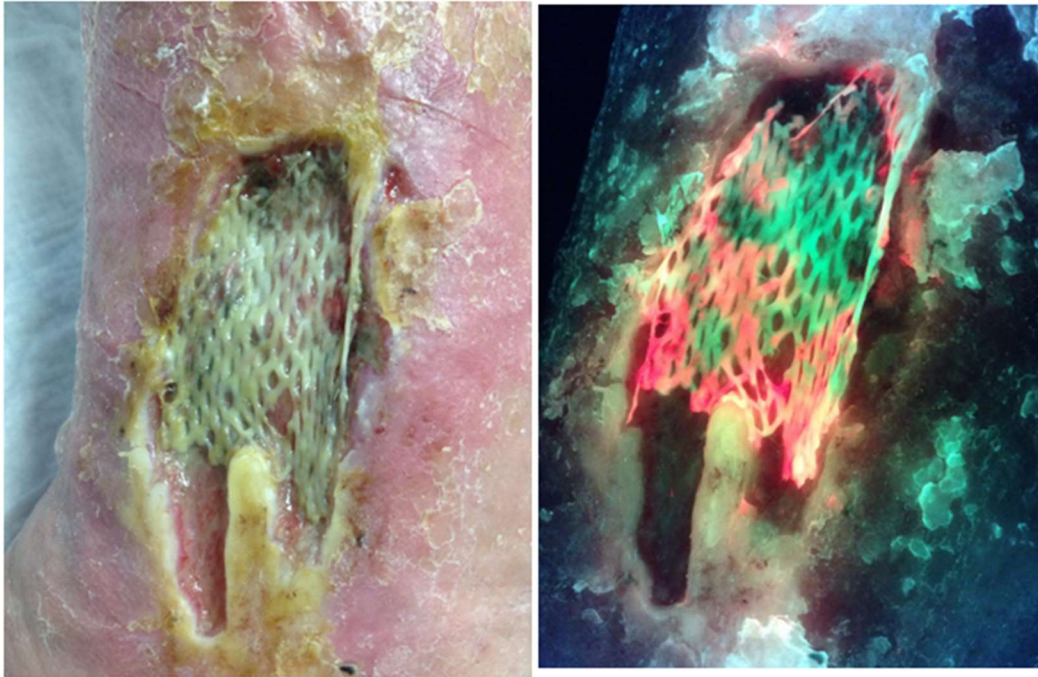
Figure 3: Standard and Fluorescence images one week following application of a CTP showing red fluorescence associated with the CTP failure.

This manuscript proposes a straightforward evidence-based method to establish an ASP in the outpatient wound care center, using point-of -care fluorescence imaging to visualize high bacterial load.   Data on topical antimicrobial and antibiotic use will be collected from advanced wound care centers across the United States. The pandemic has delayed implementation; however, antimicrobial stewardship will soon become part of standard wound center reporting. The ultimate goal is for wound care centers to share this information. The cumulative data on antimicrobial use will improve patient care and inform future ASP interventions.

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