

## Antimicrobial stewardship in wound care: a Position Paper from the British Society for Antimicrobial Chemotherapy and European Wound Management Association

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**Background:** With the growing global problem of antibiotic resistance it is crucial that clinicians use antibiotics wisely, which largely means following the principles of antimicrobial stewardship (AMS). Treatment of various types of wounds is one of the more common reasons for prescribing antibiotics.

**Objectives:** This guidance document is aimed at providing clinicians an understanding of: the basic principles of why AMS is important in caring for patients with infected wounds; who should be involved in AMS; and how to conduct AMS for patients with infected wounds.

**Methods:** We assembled a group of experts in infectious diseases/clinical microbiology (from the British Society for Antimicrobial Chemotherapy) and wound management (from the European Wound Management Association) who, after thoroughly reviewing the available literature and holding teleconferences, jointly produced this guidance document.

**Results:** All open wounds will be colonized with bacteria, but antibiotic therapy is only required for those that are clinically infected. Therapy is usually empirical to start, but definitive therapy should be based on results of appropriately collected specimens for culture. When prescribed, it should be as narrowly focused, and administered for the shortest duration, as possible. AMS teams should be interdisciplinary, especially including specialists in infection and pharmacy, with input from administrative personnel, the treating clinicians and their patients.

**Conclusions:** Available evidence is limited, but suggests that applying principles of AMS to the care of patients with wounds should help to reduce the unnecessary use of systemic or topical antibiotic therapy and ensure the safest and most clinically effective therapy for infected wounds.

### Introduction

The world is facing a rapidly worsening crisis related to the rise in rates of resistance of bacterial pathogens to available therapeutic antimicrobial agents. As no fundamentally new classes of antibiotics have been discovered in recent decades, treatment of infections must currently rely on the available agents. However, infection-producing bacteria are increasingly developing resistance to many routinely used antibiotic groups, and even to 'last resort' agents. The spread of antibiotic-resistant bacteria has led many experts to declare this issue one of the world's most pressing public health problems.<sup>1</sup> It is thus time to review and improve how antimicrobials are used for all types of clinical problems, including for various types of wounds.

### Why we need antimicrobial stewardship

Factors contributing to the growth of antibiotic resistance are complex, but clearly the rate of antibiotic resistance is directly related to the level of antibiotic use. This document is concerned only with clinical prescribing for humans, an area over which clinicians have more control and in which improvements may occur relatively quickly. Clinicians, as well as the public, must understand that antibiotic consumption is associated with the development of antibiotic resistance at not only the individual patient level, but also at community, national and regional levels.<sup>2</sup> Prior treatment of a patient with commonly used antibiotics greatly increases that person's risk of infection with an antibiotic-resistant organism, which is directly responsible for increases in morbidity, length of hospitalization, mortality and cost of healthcare.<sup>3,4</sup>

**Table 1.** Key factors contributing to antimicrobial misuse in patients with wounds

Factor	Possible solutions
Diagnostic uncertainty (is there a bacterial infection in this wound?)	Rapid diagnostic tests for presence of bacterial infection; reliable biomarkers
Clinician ignorance (when to treat with antibiotics)	Clinician education; readily available, authoritative guidelines and other resources
Clinician fear (of failing to treat properly, or of having a bad outcome)	Clinician education and reassurance; administrative (including legal) support
Patient demands (for unnecessary antibiotic therapy)	Patient education, using various individual and group approaches

Studies across the globe have consistently revealed that about 80% of antibiotic courses, and 20% of all antibiotics administered, are prescribed in the community or ambulatory setting. In both the outpatient and inpatient settings, up to 50% of these treatment courses are unnecessary or inappropriate.<sup>5</sup> Table 1 summarizes some of the key factors specifically contributing to antimicrobial misuse in patients with wounds. In addition to driving resistance, inappropriate antibiotic prescribing is associated with avoidable drug-related adverse events, other collateral ecological damage such as *Clostridium difficile* disease, and unnecessary financial costs. The rate of antibiotic misuse in long-term care facilities, where highly vulnerable patients with wounds frequently reside, may be especially high.<sup>6</sup>

These data highlight the urgent need for more prudent antibiotic prescribing, both for prophylaxis and treatment. Antibiotics are perhaps the only drugs that inevitably become less effective with use, and that have potential adverse effects on persons for whom they are not prescribed. Thus, the concept of 'stewardship', the ethical and responsible planning and management of a resource, has gained clinical, political and governmental traction over the last decade. Antimicrobial stewardship (AMS) is an interprofessional effort across the continuum of a patient's care that involves timely and optimal selection of antimicrobial agents, their doses and the duration of their use; the aim is to achieve the best clinical outcome with minimal toxicity to the patient and the environment.<sup>7</sup> AMS programmes have been shown to achieve these aims, especially if they obtain commitment from organization leaders, seek accountability for actions and outcomes, include members with antibiotic agent expertise, actively engage in implementing changes, track and report the outcomes of these actions, and educate all involved healthcare workers and patients about the optimal use of antimicrobials.<sup>8</sup> In a range of settings implementing an AMS programme has been associated with reduced rates of antibiotic resistance, fewer *C. difficile* infections, better clinical outcomes and lower financial costs.<sup>9-11</sup>

In simple terms AMS generally includes: (i) avoiding prescribing antimicrobials when they are not indicated (e.g. a non-infectious problem or a non-bacterial infection); (ii) prescribing an appropriate regimen when antimicrobial therapy is indicated [i.e. the narrowest spectrum for the likely or proven pathogen(s)]; (iii) ordering therapy for the correct duration (i.e. just long enough to achieve resolution of the signs and symptoms used to diagnose infection), at the optimal dose and by the appropriate route; and (iv) using an agent that has the least risk for adverse effects for the patient and the community (see Table 2).<sup>12</sup> It is also clear that improving antibiotic use will require increased accountability and transparency at the societal level.<sup>13</sup>

There are two main types of approaches to AMS. *Persuasive* methods, aimed at educating the clinician and encouraging optimal treatment, broadly advise clinicians about how to prescribe, or give feedback on their prescribing. *Restrictive* methods, on the contrary, administratively constrain how clinicians may prescribe, such as by limiting access to specific antibiotic agents, or by instituting automatic stop orders or time limits for antibiotic treatments. One hybrid type of intervention encourages all clinicians to take an 'antibiotic time-out' about 48 h after prescribing a regimen to review whether or not the patient has an infection, if they are on the most appropriate antibiotic regimen and for how long the therapy should continue. A meta-analysis of 89 studies from 19 countries found that each approach could improve prescribing, reduce antibiotic resistance and decrease the number of hospital-acquired infections.<sup>9</sup> Available data suggest that persuasive interventions are less effective in the short term than restrictive methods, but may have a greater long-term effect on prescribing practices.

Unfortunately, available studies of AMS interventions provide few data on potential harms of the programme, long-term sustainability, or which of the multiple components are the most important. Furthermore, most studies of AMS programmes are reported from resource-rich settings and inpatient facilities, but evidence of their effectiveness in outpatient settings where most antibiotic prescribing occurs is emerging.<sup>14</sup> AMS interventions are most useful when determined by the type, scale and context of the problems uncovered by audits. The 'Start Smart and Then Focus' programme promulgated by Public Health England provides an algorithmic approach, which may be helpful in engaging clinicians in daily stewardship activity and can be adopted or adapted (as we have done in Figure 1) to the local clinical, geographical and healthcare setting.<sup>15</sup>

Whilst the AMS approach is generic to prescribing for all types of infections, a range of recommendations has been developed for specific syndromes. Although skin and soft tissue infections are among the most common for which antibiotics are prescribed, we have been unable to find any published guidance for prudent antimicrobial therapy practice for this indication. In particular, we know of no guidelines for the subset of patients with infected wounds, which represent a huge clinical and economic burden and pose special problems both in diagnosis and treatment. For example, wound infections are frequently polymicrobial, thus requiring broad-spectrum antimicrobial regimens, and most wounds take many weeks (or even months) to heal. Some clinicians think that they should continue antibiotic therapy until healing occurs, but no evidence supports this belief.<sup>16</sup> Furthermore, because wounds are frequently recurrently infected, these patients are often exposed to repeated courses of therapy.

**Table 2.** Overview of optimizing antibiotic therapy for wounds

Only prescribe antibiotics for wounds that are clinically infected	<ul style="list-style-type: none"> <li>No antibiotics for clinically uninfected colonized or contaminated wounds</li> <li>No antibiotics for non-bacterial infections</li> </ul>	<ul style="list-style-type: none"> <li>Wound infection should usually be diagnosed clinically</li> <li>Occasionally diagnosed by quantitative bacteriology (<math>\geq 10^5</math> cfu/g tissue)</li> </ul>
Select empirical antibiotic therapy based on available clinical and laboratory data	<ul style="list-style-type: none"> <li>Cover likeliest pathogens, based on clinical presentation and local antibiotic resistance data</li> <li>Aim for narrow-spectrum regimen, unless severe illness or immunocompromised host</li> </ul>	<ul style="list-style-type: none"> <li>Obtain optimal specimens for culture before starting therapy</li> <li>If patient clinically stable, consider discontinuing any active antibiotic before taking culture</li> </ul>
Revise (and constrain) therapy based on clinical response and culture/susceptibility results	<ul style="list-style-type: none"> <li>If clinically responding, attempt to narrow antimicrobial spectrum; change regimen from parenteral to oral</li> <li>Consider switch to topical therapy or non-antibiotic antimicrobials</li> </ul>	<ul style="list-style-type: none"> <li>Often unnecessary to treat low virulence bacterial species in a polymicrobial infection</li> </ul>
Provide antibiotic therapy for the shortest duration needed to treat infection	<ul style="list-style-type: none"> <li>Treat only until all clinical evidence of infection has resolved, irrespective of wound healing</li> </ul>	<ul style="list-style-type: none"> <li>Duration of therapy usually 1–2 weeks for soft tissue, about 6 weeks for bone infection</li> </ul>

Additionally, while some wounds that show evidence of inflammation may not be infected, there is currently no universally accepted criterion standard for diagnosing infection. These factors frequently lead to antibiotic misuse among patients with both infected and uninfected wounds, ultimately leading to antibiotic-resistant infections.<sup>17</sup>

A study in Sweden, where the consensus is to restrict antibiotic therapy of wounds, found that among 707 patients seen in various inpatient and outpatient settings, 27% were receiving systemic antibiotic therapy, a rate of antibiotic therapy over 10 times higher than that for the whole population of the study region.<sup>18</sup> Another report from Sweden, where a mandatory national registry of ulcer treatment was subsequently established,<sup>19</sup> documented widespread unnecessary use of systemic antibiotics in the management of chronic wounds. But, instituting the registry led to a reduction in patients receiving antibiotic treatment for these wounds from 71% to 29%.<sup>19</sup>

In preparing this document we assembled a multidisciplinary group with experience in wound infections to develop pragmatic guidance on optimizing antimicrobial therapies for wounds. This guidance is not intended to be a comprehensive or systematic review of the literature, nor a set of highly regimented recommendations. Rather, it is a joint, interdisciplinary undertaking of the European Wound Management Association (EWMA) and the British Society for Antimicrobial Chemotherapy (BSAC) that aims to use well-established principles of wound management, antibiotic treatment and stewardship to provide practical guidance to the various primary care and specialty clinicians and the extended healthcare team who treat patients with any type of wound.

## Who should be involved in AMS for wounds?

### Teams: AMS and wound care

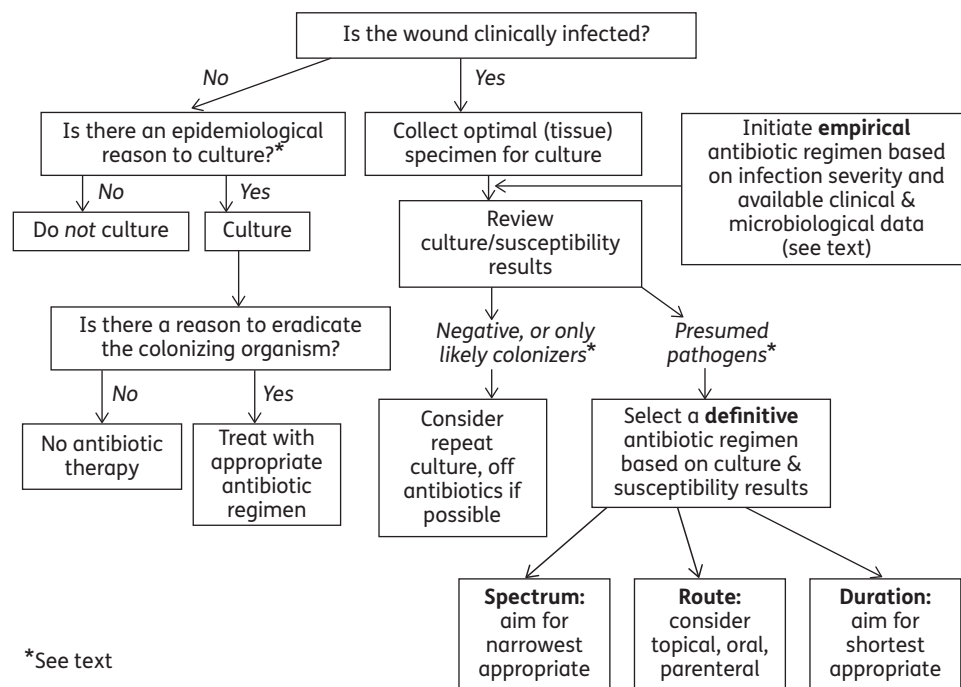
When possible, an interdisciplinary team of specialists should undertake AMS. In the hospital setting this usually includes an

infectious diseases physician or clinical microbiologist, an infection control manager and a pharmacist. The team should develop institutional policies, while also recommending best-treatment options for individual patients. The idea of an AMS team is not new,<sup>20</sup> but the rules for how it will run differ based on the institution's needs and resources. Unfortunately, these teams are infrequently available in the outpatient setting. AMS teams often work in conjunction with a team devoted to improving wound care, often for pressure or diabetic foot ulcers. These wound teams usually comprise clinicians (e.g. specialized nurses, physicians and surgeons), microbiologists, pharmacists, prosthetists/orthotists and others. The specific training of the individual is often less important than their enthusiasm for the team's goals. The activities and structure of any team must be flexible and function within constraints imposed by other hospital activities.

Given the variety and frequent changeover of clinicians who may care for a patient, wound care teams must devise a method (preferably electronic, with standardized measurements and photographs) to document the wound's status and the team's plan of care. The benefits of teamwork can be undermined by interprofessional rivalries and miscommunication, sometimes related to a lack of commonly agreed terminology. Members of the AMS programme must maintain their own education in the field as well as impart up-to-date knowledge to other clinicians and to patients.

### Patients

Healthcare workers must remember that the patient is a crucial member of the teams caring for them. The clinicians must both educate and empower the patient (or a responsible caregiver) to ensure they understand and agree with the treatment plan. The patient must be initially, then continually, apprised of the issues related to wound care during the course of treatment. Unfortunately, many patients have come to believe that antibiotic therapy is beneficial, even necessary, for treating their wounds. If the clinician suggests otherwise there is the potential for conflict



**Figure 1.** Algorithmic approach to antibiotic therapy for wounds.

and reduced patient satisfaction with their care.<sup>21</sup> While the clinician may decide to give in to the patient's expectation, experience suggests that most patients will respond positively to reassurance and an explanation that for their wound the risks of antibiotic therapy (both for them, and for society as a whole) are greater than any potential benefits. Patients should also be encouraged to inform their clinicians about any treatments (including antimicrobials not prescribed to them for this wound, or over-the-counter or folk remedies) they have recently used and any problems they think they may have in adhering to the treatment plan.

### Clinicians

We used the term 'clinician' to describe any healthcare professional who has been educated, trained and certified to provide direct patient care. Their key goals in treating a wound are relieving discomfort, eradicating any infection and accelerating wound healing, while avoiding adverse effects, controlling costs, forestalling re-infection, and averting administrative or legal censure for failing to meet the 'standard of care' with their treatment. In some countries specially trained non-medical-doctor clinicians, e.g. podiatrists/chiropractors, advanced practice nurses or pharmacists, can prescribe antibiotic therapy, but access to antiseptics is usually unrestricted.

### How to conduct AMS for patients with wounds

Even in centres that have an AMS team, any healthcare worker who deals with wounds should be familiar with the basic principles of this process. To this end, it is essential that all clinicians caring for patients with wounds know how to accurately diagnose the presence or absence of infection. In complex cases or with patients with comorbidities, it may be helpful for an inexperienced clinician to

seek consultation for this task from a wound specialist. Clinicians should, of course, make antimicrobial prescribing decisions in individual patients in the context of the broader AMS programme, as well as in collaboration with other hospital or outpatient clinical management teams.<sup>22,23</sup> Figure 1 presents a simplified algorithmic approach for antimicrobial therapy of wounds.

### Diagnosing infection

The treating clinician should assess for the presence of local or systemic evidence of infection at the first, and every subsequent, wound assessment. Wound infection is primarily diagnosed by clinical findings, usually supported by microbiological data. Culturing clinically infected wounds is helpful to define the pathogens present and their antibiotic susceptibilities. Clinicians should not, however, prescribe antibiotics just because organisms grow from a wound culture, as all open wounds become colonized.

The key diagnostic features of wound infection are the classic signs of inflammation: redness or erythema (rubor), warmth (calor); swelling or induration (tumor); pain or tenderness (dolor); and, pus or purulent secretions. Neuropathy, vascular insufficiency and various types of immunodeficiency may be associated with abnormal local inflammatory responses, thus potentially masking (or mimicking) these diagnostic findings. In these settings, it may be necessary to assess so-called 'secondary' or 'intermediate' signs and symptoms suggesting wound infection, such as friable or discoloured granulation tissue, pocketing, undermining of the ulcer rim or foul odour. Systemic signs or symptoms (e.g. fever, chills, altered mentation) or elevated inflammatory markers (e.g. leukocytes, C-reactive protein, erythrocyte sedimentation rate) are often absent with a wound infection. Clinicians must seek any evidence of underlying deep tissue infection (e.g. of muscle, tendon, joint, bone), as well as involvement of any prosthetic or implanted material, as these usually require surgical

intervention. A thorough evaluation allows the clinician to determine the need for advanced imaging tests, surgical procedures and the choice of antimicrobials.

### Specimen collection

There is generally no need to culture a clinically uninfected wound, as these do not require antimicrobial therapy. All clinically infected wounds should be cultured, however, preferably by obtaining tissue (either by curettage or biopsy), which provides more sensitive and specific results than swabbing<sup>24,25</sup> To lessen the likelihood of identifying colonizers (rather than pathogens), clinicians should cleanse (with a non-bactericidal agent) and debride the wound before collecting a specimen for culture. Managers should remove organizational barriers to tissue sampling, e.g. lack of required collection and transport equipment, or of a clinician with sampling expertise. To avoid false-negative cultures, it is best (if possible) to collect a specimen for culture before starting antibiotic therapy. The advantages of avoiding inappropriate antimicrobial therapy by proper wound sampling outweigh any potential increase in short-term organizational costs. For a patient exhibiting signs of systemic inflammatory response syndrome the clinician should order blood cultures. Although wound infections are infrequently associated with bacteraemia, if present it usually requires hospitalization, along with intravenous and longer duration antibiotic therapy.<sup>26</sup> When there is suspicion that a wound may be complicated by osteomyelitis the clinician should consider obtaining a bone culture. These often reveal different results (usually fewer pathogens) than cultures of superficial or even deep soft tissue.

### Specimen processing and reporting

Once collected, the specimen for culture must be rapidly and properly transported to the clinical microbiology laboratory, accompanied by key clinical details, especially regarding recent or current antibiotic therapy. The laboratory must process the specimen quickly and report the results in understandable language. Some laboratories reasonably believe that to reduce the likelihood of inappropriate antibiotic therapy they should sometimes selectively restrict their reporting of isolated organisms or their antibiotic susceptibility results.<sup>22</sup> We believe that in settings where the clinician has, or has access to, expertise in clinical microbiology, laboratories should report all isolates from properly collected specimens. They should certainly report the presence of likely pathogenic organisms (e.g. *S. aureus*,  $\beta$ -haemolytic streptococci) and the susceptibility results for 'first line' antimicrobials against these (e.g. semi-synthetic penicillins and macrolides). Susceptibility to advanced-generation cephalosporins or broader-spectrum penicillin/ $\beta$ -lactamase inhibitor combinations might be 'suppressed', to discourage their unnecessary use. Although any organism isolated from a properly collected specimen may be a pathogen, it may be appropriate for clinical microbiologists to suggest that some (e.g. corynebacteria, enterococci, coliforms, obligate anaerobes), especially if identified by highly sensitive molecular methods, are likely to be colonizers. Additional culture and susceptibility results should, of course, be available following discussion between the clinician and infection specialist.

Recently there have been reports of various molecular based techniques for diagnosis of bacterial infection in wounds.<sup>27,28</sup>

These may contribute to AMS by providing more rapid identification of causative pathogens, sometimes of their antibiotic resistance profiles, and perhaps the presence of virulence factors.<sup>29</sup> This potentially facilitates rapid selection of the most appropriate, narrowly targeted antibiotic regimen. However, while rapid molecular tests for pathogens to constrain unnecessary antibiotic therapy are useful for infections diagnosed microbiologically, they are less helpful for clinically diagnosed wound infections. Newer molecular microbiological techniques often disclose more pathogens than standard cultures, but we as yet do not know the clinical significance of this additional information.<sup>30</sup>

### Indications for antibiotic therapy

A common antibiotic prescribing error is treating a patient with a superficial uninfamed wound from whom commensal bacteria are isolated (e.g. coagulase-negative *Staphylococcus*) or from whom clinically irrelevant bacteria or fungi (e.g. enterococci, coliforms or *Candida*) have 'overgrown' the wound during ongoing antibiotic therapy. No evidence supports that treatment with antibiotics in such situations either improves wound healing or prevents the development of clinical infection.<sup>16</sup> Microbiological investigations for a clinically uninfected wound are needed only when seeking evidence of colonization with an epidemiologically important pathogen (e.g. MRSA, VRE or carbapenemase-producing Enterobacteriaceae). Knowing the carriage status of a patient at high risk for multidrug-resistant colonization may help determine the need for source isolation or short course decolonization therapy, or help select the appropriate therapy should the patient later develop evidence of wound infection.<sup>31,32</sup>

## Approach to clinical management of wound infection

### Empirical and definitive therapy

Antibiotic therapy is usually initially *empirical*, i.e. based on best guess of the causative pathogens and their antibiotic susceptibility, informed by available clinical and epidemiological data. Later *definitive* therapy is based on available culture and susceptibility results, and the clinical response to empirical therapy. Key factors in selecting empirical therapy include: the severity of the infection; any history suggesting likely pathogens (e.g. exposure to animals, recent travel, admission to a healthcare facility); recent antibiotic therapy; and knowing local antibiotic resistance data and the institution's AMS strategy.<sup>33</sup> The treating clinician should document the classification of the wound, the clinical severity of infection, and any diagnostic uncertainties and further diagnostic tests planned.

While risk stratification guidelines, such as those produced by the Infectious Diseases Society of America for skin and soft tissue infections,<sup>31</sup> MRSA<sup>34</sup> and diabetic foot infections,<sup>35</sup> are helpful, antimicrobial choices should be tailored to local circumstances. Empirical antibiotic therapy for virtually all infected wounds should be active against *S. aureus* (with consideration for the likelihood of MRSA), as it is the most commonly isolated pathogen in most settings. Additional coverage for other organisms (potentially including aerobic Gram-negative and anaerobic organisms) may be appropriate for severe infections or for patients with findings that suggest these organisms. Selecting an antibiotic

regimen, including the dose and route of administration, depends on many factors. For an acute, severe (e.g. accompanied by sepsis or rapid progression) wound infection, intravenous therapy is usually appropriate, often with a combination of bactericidal agents. When the infection has clinically responded and microbiological results are available, consider simplification (narrowing the spectrum of therapy), changing from intravenous to oral ('switch') therapy with an agent with good orally bioavailability, or stopping therapy if an alternative (non-infectious) cause has been established.<sup>13</sup>

### The use of topical antimicrobials

While systemic antibiotic therapy is appropriate for most clinically infected wounds, for superficial, mild infections topical antimicrobial (antibiotic and non-antibiotic) agents may have several potential benefits.<sup>36</sup> Most noteworthy: a small amount can achieve high levels directly at the site of infection; it avoids systemic adverse effects; and, it allows use of agents that cannot be administered systemically. There is much regional and geographical variation in the use of topical antibiotics, and in resistance rates of pathogens to these agents. We advise avoiding using antibiotics (as opposed to antiseptics) topically for treating wound infections as there is limited evidence of their effectiveness and they often select for resistant colonizing bacteria. Furthermore, topical treatment may cause peri-wound skin irritation, rash, eczema or impairment of wound healing.<sup>37</sup> Concerns also remain about possible cytotoxic effects of topical antimicrobials on the wound bed, especially with long-term treatment.<sup>19,36</sup> A few topical antibiotics (e.g. fusidic acid, mupirocin, neomycin) may be appropriate to treat localized acute superficial skin infections, such as impetigo and folliculitis, but almost all other clinically infected wounds require systemic antibiotic therapy.<sup>38,39</sup> Topical metronidazole may be beneficial in reducing wound odour, but the evidence is weak.<sup>40</sup>

Non-antibiotic antimicrobials are widely used in wound care, notwithstanding the limited data supporting their usefulness. These include antiseptics (e.g. chlorhexidine, povidone or cadexomer iodine), heavy metals [e.g. silver, mercury (mercurochrome)] and natural products (e.g. honey, charcoal). Topical antimicrobials

may be helpful where there is localized infection of chronic wounds,<sup>37</sup> although some antiseptics may delay healing.<sup>36,38</sup> For wounds with secondary clinical signs of localized infection<sup>41,42</sup> applying topical non-antibiotic agents after adequate debridement may be useful, perhaps by suppressing biofilm formation.<sup>41</sup> Table 3 summarizes our suggested approach to topical antimicrobial therapy for wounds.

Cleaning and debriding of necrotic, sloughy or inflammatory material likely accelerates wound healing and is usually best achieved by mechanical means. Investigators are now seeking non-antibiotic approaches to killing bacteria in wounds. One recently described technique employs compounds that work by slowly releasing reactive oxygen radicals over a prolonged period.<sup>43,44</sup> This can be accomplished with medical honey, which is highly antimicrobial, including against multiresistant organisms.<sup>45-47</sup>

### Bone infection

Infection in bone typically develops by contiguous spread from overlying soft tissue. Osteomyelitis is usually more difficult to eradicate than soft tissue infection, but in some cases can be treated with prolonged (~6 weeks) antibiotic therapy. Most authorities, however, prefer surgical removal of infected and necrotic bone, if possible. Initial antibiotic treatment of osteomyelitis is usually given intravenously, but in most cases this can be quickly switched to (or in non-severe infections initiated with) oral therapy if there is an appropriate, bioavailable agent for the isolated pathogen(s). Bioavailability and bone penetration of most oral  $\beta$ -lactam antibiotics is limited, but that of fluoroquinolones, rifampicin, tetracyclines, oxazolidinones and clindamycin is good.<sup>48,49</sup> Of note, therapy with certain agents (e.g. rifampicin, sodium fusidate, trimethoprim) must be in combination with another active agent (especially against *S. aureus*) to avoid rapid development of resistant strains.

### Additional aspects of AMS in relation to wound management

Key stakeholders in local wound management and AMS programmes should optimally produce, or at least assess and

**Table 3.** Approach to using topical antimicrobial therapy for treating wounds<sup>a</sup> (reproduced from reference 36)

Infection status	Definition	Consequences	Antimicrobial therapy
Uninfected	No classical <sup>b</sup> or secondary <sup>c</sup> clinical evidence of infection	None	None
Uncertain	Only secondary clinical evidence of infection, or quantitative culture with $\geq 10^5$ cfu/g of tissue	Possibly slowed or absent wound healing, malodour, wound discomfort	Consider short-term topical antiseptic therapy
Infected	Classical <sup>c</sup> clinical signs or symptoms of inflammation	Progression of infection, failure of wound healing, wound discomfort	Systemic <sup>d</sup> antibiotic therapy (with or without topical antiseptic)

<sup>a</sup>Please note this is in addition to the usual required wound care (e.g. debridement, off-loading, proper dressings, and correcting critical limb ischaemia, malnutrition, hyperglycaemia or other metabolic problems).

<sup>b</sup>Purulent discharge, or erythema, warmth, pain or tenderness, or induration.

<sup>c</sup>Non-purulent (serous or sanguineous) exudate, discoloured or friable (easily bleeding) granulation tissue, breakdown or 'pocketing' at the base of the wound, or abnormally foul odour.

<sup>d</sup>Oral or parenteral, depending on the severity of the infection and the agent(s) required.

**Table 4.** Key opportunities for antimicrobial stewardship in wound management (see text for details)

Opportunity	Good practice	Antimicrobial stewardship goal
Diagnosis	Seek the presence of any clinical signs or symptoms of infection, and document the severity and extent/depth of the wound	Avoid prescribing antibiotics for uninfected wounds and optimize early management in serious infection
	For infected wounds, obtain appropriate specimen(s) for microbiological analysis, rapidly transport them to, and communicate with, the microbiology laboratory	Optimize diagnostic sensitivity and specificity of wound cultures, and ensure proper interpretation of the results
	Laboratory reports should include all likely pathogens, but possibly restrict susceptibility reporting	Minimize unnecessary use of antibiotics, optimize antibiotic choice, and promote use of narrow-spectrum regimens
Surgical management	Consider, and undertake when indicated, wound debridement and limb revascularization	Optimize collection of specimens for culture, antibiotic delivery and wound healing
Empirical antibiotic choice	Use locally agreed guidance, endorsed by the AMS programme, stratified for severity of infection	Avoid overly broad-spectrum regimens, aiming to minimize risk of development of antimicrobial resistance, drug-related adverse effects, and <i>Clostridium difficile</i> disease
Antibiotic review (definitive therapy)	Follow criteria for switching from parenteral to oral therapy, de-escalating (narrowing) spectrum, and limiting duration of therapy	
Antibiotic prescribing surveillance: overall and targeted	Institute institutional surveillance and audit programmes, with review and feedback of key data to treating clinicians and managers, and responses to suboptimal prescribing trends	Promote awareness of risks of inappropriate antimicrobial therapy and use benchmarking (comparing with local and national data) to help drive quality improvement.
	Review prescribing: by individual providers; for individual patients; and, for issues of local practice that raise concerns	Quality improvement in clinical practice through broadly based clinician and case review
Education	Ensure widespread familiarity with, and understanding of, programmes for proper wound infection management and antibiotic therapy, by requiring participation of all clinical staff in educational and quality improvement exercises	Promote awareness of, and local development and adherence to, AMS guidance and optimization of antibiotic therapy and treatment outcomes.

AMS, antimicrobial stewardship.

oversee, guidelines for management of wound infections. A local quality improvement programme should assess key components of clinical management of wounds, such as regularly reviewing and reporting on the appropriateness of both outpatient and inpatient use of antibiotics. Sites should attempt to compare their results against their own previous performance as well as against other similar sites. Benchmarking can drive improvement in compliance with guidance documents.<sup>50,51</sup> Quantitative review of prescribing is typically calculated using dispensing data, usually adjusted for activity.<sup>52,53</sup> While these data do not describe individual patient prescribing, they provide information on antibiotic pressure and prescribing trends that help to monitor adverse antibiotic outcomes, particularly the development of resistance.<sup>53</sup>

Qualitative review of antibiotic prescribing gives complementary information on clinical practice. Some key areas worthy of audit may include: frequency of examining for, and recording clinical signs of wound infection; recording specific infectious syndrome diagnoses; explaining the choice of an antibiotic regimen; compliance with local policies; and documenting the planned duration of therapy.<sup>54,55</sup> Conducting a point prevalence survey can

provide such information.<sup>56</sup> In parallel, there should be regular programmed reviews of antibiotic-associated adverse events, e.g. *C. difficile* infection or treatment-related acute kidney injury.<sup>57-59</sup> Healthcare organizations and stewardship teams have found that using various process and outcomes measures for prescribing can improve performance.<sup>51</sup> In these areas, and most other aspects of AMS, nurses play a crucial role.<sup>60,61</sup>

Finally, regular programmed education and peer support are essential to ensure all members of the multidisciplinary team are familiar with local antimicrobial guidance and key surveillance data. Understanding and acceptance of the rationale for stewardship of antibiotics underpins compliance. Stewardship programmes should support easy and affordable access to high-quality educational sessions and materials. Web-based educational packages on stewardship are becoming available for both medical and non-medical healthcare staff.<sup>62-65</sup>

There is much we still need to learn about caring for infected wounds, but the current state of knowledge is sufficient to offer some basic principles of management. Table 4 provides a brief summary of what we see as key opportunities for antimicrobial stewardship in wound management.

### Suggested research areas for AMS in wound care

- Develop more accurate methods to determine whether or not a wound is infected.
- Investigate the need to cover all, most or only selected pathogens in polymicrobial wound infections.
- Examine the efficacy and safety of various types of antimicrobial dressings on wounds.
- Investigate whether or not heavy microbial colonization plays a pathogenic role, and if so, the potential benefits of various methods to lower the bioburden.
- Investigate simple ways to detect biofilm in wounds, determine how best to remove it and whether or not removal improves resolution of infection or rate of healing.
- Investigate the effectiveness of shorter durations of antibiotic therapy on resolution of infection.
- Determine whether or not rapid diagnostic tests detecting the type of bacteria, the presence of virulence factors or antibiotic resistance genes can help clinicians in narrowing the spectrum of empirical antibiotic therapy.
- Conduct clinical studies to test the value of various antiseptics in treating colonized and infected wounds, especially to see if these can reduce the need for antibiotic therapy.

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