Controversies in Long Term Care

Swab Culture of Purulent Skin Infection to Detect Infection or Colonization With Antibiotic-Resistant Bacteria

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A B S T R A C T

Prescribing systemic antibiotics without susceptibility testing has significant shortcomings, especially in long term care facilities with high rates of multidrug-resistant organisms (MDROs) including methicillin-resistant Staphylococcus aureus. Tissue biopsy or aspiration sampling of infected tissue is the “gold standard” for culture of skin and soft tissue infection and is especially important with serious infection, systemic toxicity, or failure of initial therapy. Swab cultures are probably the most commonly used method to determine the resistance pattern of skin pathogens treated in nursing home residents. However, they are controversial, especially when obtained from chronic wounds. The culture may be obtained from an uninfected wound and lead to unnecessary antibiotic therapy. If material superficial to the infected living tissue is sampled, colonizers may be isolated. This report is focused on swab culture obtained by the Levine technique, after debridement or cleaning down to viable tissue when an acute purulent skin infection has been diagnosed based on clinical criteria. Swab cultures should not be used to determine if a wound is acutely infected; rather the role may be to identify potential pathogens when deep tissue biopsy is not elected. The swab culture may identify the pathogen or overlying MDRO colonization, a risk factor for MDRO infection. MDRO isolation should heighten the clinician’s level of concern if the prescribed antibiotic did not “cover” the MDRO or potential pathogen that was isolated. Properly performed swab cultures could play a role in the identification of methicillin-resistant Staphylococcus aureus/MDRO infections treated in nursing homes.

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One of the authors reviewed a legal case in which a resident almost lost a leg because debridement and culture of an infected wound were not performed. Later, when the infection was severe, the resident finally received debridement and culture. None of the infecting organisms were sensitive to the empiric antibiotics prescribed. It is not uncommon for nursing home clinicians to rely on empiric systemic antibiotics and to forego culture.

Skin and soft tissue infections (SSTIs) are the third most common infection in nursing homes.1 This report addresses whether antibiotic therapy for mild acute purulent SSTI treated in the nursing home should be empiric or proceeded by culture. Perhaps the most common type of acute purulent SSTI encountered in nursing homes develops within a chronic wound. These infections are considered to be “complicated.”

According to the Infectious Disease Society of America (IDSA), mild acute infections are defined as those in which cellulitis is limited to the skin or superficial subcutaneous tissue; and extends ≤2 cm around an ulcer without systemic manifestations.2 Practitioners should be aware of the fact that chronic venous stasis or other conditions may produce an inflammatory dermatitis that can be confused with cellulitis and lead to unnecessary antibiotic treatment.3 Moderate to severe infections include cellulitis extending >2 cm around an ulcer, lymphangitic streaking, spread beneath the superficial fascia, deep-tissue abscess (futulence, induration), gangrene/necrosis, and involvement of muscle, tendon, joint or bone, systemic toxicity, or metabolic instability (e.g., fever, chills, tachycardia, hypotension, vomiting, confusion, leukocytosis, acidosis, severe hyperglycemia, or azotemia).3 A wound may require careful inspection following debridement initially and over time to determine if acute infection exists and which structures are involved.

Given significant rates of community-associated methicillin-resistant Staphylococcus aureus (MRSA) skin infection; the recently
published IDSA Guideline on the Treatment of MRSA Infections recommends obtaining cultures to guide systemic antibiotic therapy in purulent skin infections (e.g., associated with purulent drainage or exudate). In addition, the IDSA Guideline on the Management of Diabetic Foot Infections recommends obtaining cultures prior to starting antibiotic therapy. On the other hand, the IDSA long term care (LTC) guideline seems to favor starting initial antibiotic therapy in mild skin infections without obtaining a culture: Gram stain and bacterial cultures “may be appropriate in special circumstances in which unusual pathogens are suspected” based on the opinions of respected authorities. The AMDA Guideline on Pressure Ulcers states: “Surface swab cultures are not recommended because they cannot differentiate infection from contamination or colonization.” We agree that a swab culture should not be used to determine if a wound is acutely infected; rather, the role may be to identify potential pathogens in a wound that is acutely infected based on clinical assessment when deep tissue biopsy is not available or elected. In our opinion, nursing home clinicians who treat purulent skin infections with systemic antibiotics without obtaining a culture do so based on expert opinion only. Expert opinion is divided, creating a “Clinical Controversy.”

Empiricism has significant shortcomings, especially in LTC facilities with high rates of multidrug-resistant organisms (MDROs). MRSA is a prominent pathogen in acute SSTI. Empiric coverage of *S. aureus* is recommended in a large proportion of skin infections regardless of severity. *Enterococcus, Pseudomonas aeruginosa,* and other gram-negative rods may also express resistance to commonly used antibiotics. Residents with MDRO/MRSA infections may receive antibiotics that fail to cover the MDRO with disease progression. On the other hand, if the empiric antibiotic “covers” MDRO, lack of culture results precludes de-escalation of broad-spectrum antibiotic therapy. This will lead to unnecessary antibiotic pressure and selection of resistant organisms.

Biopsy of viable tissue and/or aspiration of infected secretions represents the gold standard for the bacteriologic diagnosis of SSTI. These techniques are especially important in serious infection, systemic toxicity, or failure of initial therapy. The IDSA Clinical Practice Guideline (CPG) for the diagnosis and management of SSTI states that: “Needle aspiration and punch biopsy specimens as well as requests for a surgical consultation for inspection, exploration, and/or drainage” should be performed in severe SSTI. On the other hand, mild acute wound infection is often managed in nursing homes without tissue biopsy or aseptic collection of infected material through intact skin by aspiration. In reality, the clinician must choose to prescribe systemic antibiotics empirically or perform a swab culture. This report is focused on swab culture obtained by the Levine technique after debridement or cleaning down to viable tissue. Data are sparse. Swab culture should not be used to determine if the wound is acutely infected but rather the role is to identify potential pathogens in a wound that is acutely infected based on clinical assessment when deep tissue biopsy is not elected. A properly performed swab culture may be especially relevant in the detection of MDRO/MRSA. The swab culture may identify the pathogen or overlying MDRO colonization, a risk factor for MDRO infection.

### Structure and Bacteriology

Aerobic gram-positive cocci are the predominant microorganisms that colonize and acutely infect breaks in the skin. *S. aureus* and the beta-hemolytic streptococci are the most commonly isolated pathogens. Chronic open wounds provide “fertile ground” for colonization with MDRO and may support complex biofilm flora with large numbers of bacteria including aerobic gram-positive cocci, enterococci, various Enterobacteriaceae, *P. aeruginosa,* sometimes other nonfermentative gram-negative rods, and obligate anaerobes. Bacterial virulence factors and local conditions (e.g., necrotic tissue, ischemia, hyperglycemia, trauma, maceration) may allow planktonic bacteria to invade surrounding living tissue to produce acute infections such as cellulitis or fasciitis. Slow growing bacteria adapted to biofilm may fail to grow using standard culture techniques that maximize the cultivation of rapidly proliferating free-living planktonic bacteria.

According to the IDSA Guideline on Foot Infection in Diabetics, acute infection should be diagnosed clinically on the basis of purulent secretions (pus) or at least two of the cardinal manifestations of inflammation (redness, warmth, swelling or induration, pain or tenderness). The AMDA pressure ulcer guideline states that purulent drainage at the ulcer site alone may not require systemic antibiotic therapy and respond to topical interventions. Wound care specialists are interested in the role that “critical colonization” or infection plays in delayed wound healing including: friability of granulation tissue. Ulcerated lesions, especially stage 3-4, must be observed carefully over time following cleaning and/or debridement to detect the cardinal manifestations of inflammation of recent onset (redness, warmth, swelling or induration, pain or tenderness). The latter criteria suggest a cellulitis that requires systemic antibiotic therapy. Infection in stage 3-4 ulcers is usually polymicrobial and may involve exposed deeper structures. The wound and surrounding tissue should be carefully assessed for signs of severe infection that could include easy dissection along the fascia by a blunt instrument, severe constant pain, tissue necrosis/sloughing, anesthesia, gas in the tissue/crepitation, or “woody” nonyielding subcutaneous tissue. Pressure ulcers and undrained cutaneous abscesses may be the source of polymicrobial MDRO bacteremia with a subtle afebrile presentation in frail residents that includes functional decline. Bacteremia may include organisms such as *Proteus, Escherichia coli,* *Pseudomonas, S. aureus* (MRSA), *Streptococcus,* and anaerobes. This report is focused on the management of mild infections treated with systemic antibiotics in the nursing home and does not address the management of severe infections in patients where tissue biopsy is clearly indicated.

### Sampling Options

Biopsy of viable tissue and/or aspiration of infected secretions are the gold standard for the diagnosis of wound infection (an infection of living tissue). However, when these samples are obtained in acute cellulitis through intact skin, a pathogen may not be isolated because the concentration of organisms is low. Causative organisms include gram-positive microorganisms (mainly *S. aureus,* group A or B streptococci, viridans streptococci, enterococci, *P. aeruginosa,* baconato bacter.,), and anaerobes. Unfortunately, few clinicians are proficient and biopsy could cause pain and/or bleeding, enlarge the wound, or introduce contaminants. A full-thickness punch biopsy may not be justified in the presence of a small or superficial wound. Biopsy is relatively contraindicated in the presence of arterial ulcers. Therefore, because of the invasiveness and limited number of qualified practitioners, swab culture is the most frequently used method to determine the resistance pattern of pathogens in acute wound infection.

Wound care nurse specialists perform conservative, sharp instrumental wound debridement to remove loosely adherent, clearly identifiable devitalized/necrotic tissue with minimal pain and bleeding. There should be a clear interface between the viable
and nonviable tissue for nurses to remove the tissue. Nurse specialists do not excise, biopsy, or place a needle into viable tissue. Advanced practice nurses might perform additional activities that could include punch biopsy or curettage of the wound base. However, only about 15% to 20% of wound care specialist nurses are advanced practice nurses. Therefore, it is likely that on-site availability of tissue biopsy, curettage, or aspiration of infected material through intact skin will remain limited in nursing homes.

Although swab cultures are the most commonly performed type of culture, they are controversial. If obtained from an uninstructed wound, they may lead to unnecessary antibiotic treatment. Cellulitis is an infection of living tissue. Specimens obtained from material overlying the infected tissue or bone may or may not reflect the infecting organisms. The swab may sample bacteria colonizing superficial eschar, slough, or necrotic tissue rather than the bacteria infecting the underlying living tissue or may fail to isolate the underlying pathogen. On the other hand, careful insertion of a swab following incision of a cutaneous abscess or from a sinus tract with purulent drainage should produce a sample with less potential surface contamination than swab culture of an infected chronic wound. Swab specimens are not optimal/suitable for culture of anaerobes and many fastidious organisms. Clinicians who use swab cultures must be aware of these potential shortcomings.

### The Levine Technique for Swab Cultures

The procedure used to obtain the swab is critical. Surface organisms contaminate all wounds. Therefore, the wound should be cleaned and irrigated (nonbacteriostatic saline) free of necrotic material, eschar, slough, or drainage prior to obtaining specimens. In some cases this will require sharp debridement. [Note: Sharp debridement may be contraindicated in arteriovenous ulcers.] The “interstitial”/tissue bioburden of pathogens might be approximated using the Levine technique, in which a 1-cm² area of viable tissue near the center of the viable wound base is sampled for 5 seconds with sufficient pressure to express fluid from within the wound tissue for culture and gram stain. Proper technique is important. Unfortunately, poor technique is often used. Invalid results might be expected if the specimen consists of debris overlying the infected living tissue.

### Swab Versus Tissue Biopsy or Curetage of the Cleaned or Debrided Acutely Infected Ulcer Base

We were able to identify only 2 studies that focused on acute infection that compared specific organisms identified by swab (following cleaning and/or debridement down to viable tissue) versus biopsy or curettage specimens. The limited data are presented next. None of the reports were generated from an LTC facility, and none included randomization of antibiotic therapy.

Pellizzer et al. cleaned and debrided the bases of 29 diabetic foot ulcers with limb-threatening acute infection in patients who had not received antibiotics for 3 weeks. Limb-threatening infection was defined by the presence of full-thickness ulcer, cellulitis >2 cm, bone or joint involvement, and systemic toxicity or serious ischemia. Pellizzer et al. compared swab specimens to punch biopsy specimens. The mean number of isolates per patient was 2.34 by swab and 2.07 by biopsy (NS). S. aureus was isolated in 10 specimens by swabbing and biopsy. The authors concluded “our experience suggests that swabbing and biopsy of the ulcer base may be equally reliable for the initial follow-up of empirical therapy in limb-threatening diabetic foot infection, provided that laboratory processing is adequate.” The authors also concluded that tissue biopsy was more reliable in wounds that were still active after 2 weeks of appropriate treatment.

Lipski et al. studied 39 ulcers in diabetic patients who had not received antibiotic therapy for 2 weeks. The ulcers were associated with acute uncomplicated lower extremity SSTI. Approximately one quarter were related to chronic ulcers. Standard bacteriology from curettage specimens was compared to swab specimens. Results were identical in 23. S. aureus was isolated in 54%. Compared to curettage, there were missing isolates in 13 swab specimens. In approximately 6, the missing isolates included anaerobes (no attempt was made to isolate anaerobes from swab specimens). In approximately 5, the missing isolates included gram-negative rods, and in 3, they included coagulase-negative staphylococci. Approximately 5 swab specimens included “contaminants” not isolated from curettage. The authors administered 2 weeks of antibiotic therapy directed against aerobic gram-positive cocci. Clinical cure occurred in 75% with improvement in an additional 16%. The authors concluded that aerobic gram-positive cocci were usually the early tissue invaders in uncomplicated previously untreated lower extremity SSTI.

### Current Guidelines Regarding Swab Culture

We reviewed current CPG regarding swab cultures and found the following, sometimes-conflicting recommendations based on expert opinion and limited data.

- **IDSA CPG for the diagnosis and treatment of diabetic foot infections states the following:** “Cleanse and debride the lesion before obtaining specimens for culture. In cases involving an open wound, obtain tissue specimens from the debrided base (whenever possible) by means of curettage (scraping with a sterile dermal curette or scalpel blade) or biopsy (bedside or operative)” [good evidence based on a controlled trial]. “Avoid swabbing undebrided ulcers or wound drainage. If swabbing the debrided wound base is the only available culture option use a swab designed for culturing aerobic and anaerobic organisms, and rapidly transport it to the laboratory” [moderate evidence from a controlled trial].

- **IDSA CPG for the evaluation of fever and infection in older adult residents of LTC facilities states the following:** “Surface swab cultures are not indicated for the diagnosis of most bacterial SSTIs” [good evidence from 1 or more well designed clinical trials, without randomization; from cohort or case-controlled analytical studies from multiple time-series; or from dramatic results from uncontrolled experiments]. “Needle aspiration (only skilled physicians should perform this procedure) or deep-tissue biopsy to obtain samples for Gram stain and culture may be appropriate in special circumstances in which unusual pathogens are suspected, fluctuant areas suggest an abscess is present, or initial antimicrobial treatment has been unsuccessful” [poor evidence and the opinion of respected authorities].

Of interest, the ISDA CPGs cited above express different conclusions regarding swab cultures, while the 2011 IDSA guideline on the management of MRSA infection does not discuss the role of swab versus tissue culture.

According to the Wound, Ostomy and Continence Nurses Society **Guideline for Management of Wounds in Patients with Lower-Extremity Arterial Disease**, “Tissue biopsy is considered the gold standard, to confirm the diagnosis of infection. Limited studies have demonstrated that noninvasive, quantitative swab cultures are a reasonable alternative to biopsies in general clinical practice settings” [consensus narrative review of several nonrandomized trials of humans selected by a systematic method]. The interested reader is encouraged to consult the details of the review performed by one of the co-authors (P.B.) that was the basis for this recommendation. The reviewer identified 19 nonrandomized studies in which swab specimens were obtained from wounds of all types.
with or without acute infection. Swab specimens were processed using quantitative and/or semiquantitative techniques.\textsuperscript{7} Quantitative technique may be more sensitive than standard semiquantitative technique.\textsuperscript{26,27} Some of the investigators used alginate swabs because of the potential bacteriostatic effect of oxygenated cotton.\textsuperscript{7}

The Institute for Clinical Systems Improvement Pressure Ulcer Prevention and Treatment's health care protocol states: “Diagnosis of wound infections is based on patient history and clinical findings. Although the gold standard for determining infection is tissue biopsy, many wounds are swab cultured for confirmation of infection. All wounds should be cleansed with a non-antiseptic solution prior to culture. The swab culture should be placed on healthy granulation tissue, pressed down and turned 360 degrees to extract fluid. Do not culture pus, slough or necrotic tissue. Infection must be treated with systemic antibiotics based on wound culture results.” [consensus statement, narrative review].\textsuperscript{15}

According to the Registered Nurses' Association of Ontario's Assessment and Management of Stage I to IV Pressure Ulcers, “To obtain a wound culture, cleanse the wound with normal saline first. Swab wound bed, not eschar, slough, exudate, or edges” [opinion of respected authorities].\textsuperscript{1,2}

\textbf{Current Practice}

We communicated with the author of a recent retrospective report, “Empiric Outpatient Therapy with Trimethoprim-Sulfamethoxazole, Cephalexin, or Clindamycin for Cellulitis,” in the American Journal of Medicine, who verified that the reported bacteriology was based on swab culture.\textsuperscript{33} An article in the New England Journal of Medicine, “MRSA Infections among Patients in the Emergency Department,” stated that “Specimens were obtained from the single largest area of infection with the use of sterile Dacron swabs.”\textsuperscript{34} Swab culture seems to be the “de facto” standard of care in publications focused on SSTI in out patients. These studies did not focus on chronic wounds, which may develop a more complex flora.\textsuperscript{2} Finally, Jenkins et al. reported, “Skin and soft tissue infections requiring hospitalization at an academic medical center” in Clinical Infectious Disease from the University of Colorado. Deep tissue samples and material from abscess cavities were cultured. The authors stated, “Needle aspirates or punch biopsies are not routinely performed at our institution.”\textsuperscript{18} Perhaps it is unrealistic to expect nursing home personnel to use biopsy or needle aspiration to determine that a mild skin infection is caused by MRSA, if these techniques are not routinely used in hospitalized patients at an academic medical center.

\textbf{Antibiotic Therapy}

Most literature on systemic antibiotic treatment of skin infection focuses on outpatients or serious infection in hospitalized patients. Clinicians are left to adapt/project these recommendations to the management of mild infections treated in the nursing home.

The 2011 IDSA guideline for the management of MRSA infections provides guidance for the management of SSTI in outpatients. The recommendations may be applicable to mild infections treated in the nursing facility. For outpatients with purulent cellulitis, therapy for MRSA is recommended pending culture results. If coverage for both beta-hemolytic streptococci and MRSA is desired, options include trimethoprim-sulfamethoxazole (TMP-SMX) or a tetracycline in combination with a beta-lactam (e.g., amoxicillin). The activity of TMP-SMX or a tetracycline against beta-hemolytic streptococci is “not well defined”; beta-hemolytic streptococci may also be resistant to erythromycin.\textsuperscript{3,4} Oral antibiotic choices (TMP/SMX, minocycline) are considered to be less reliable for methicillin-sensitive S. aureus (MSSA) than the oral agent of choice, dicloxacillin.\textsuperscript{1,4} According to the IDSA SSTI guideline, the efficacy of doxycycline/minocycline for MSSA includes “limited recent clinical experience,” while that of TMP-SMX is “poorly documented.”\textsuperscript{3} A 1992 publication, “TMP-SMX Compared with Vancomycin for the Treatment of S. aureus Infection,” found that TMP-SMX failure in serious infections occurred mostly in patients with MSSA.\textsuperscript{35} It is optimal to determine if a skin infection is caused by MRSA versus MSSA; beta-lactams are the drug of choice for MSSA.\textsuperscript{3}

If oral therapy is elected for more severe SSTI, linazolid is considered to be the drug of choice. For hospitalized patients with complicated SSTI (defined as patients with deeper soft-tissue infections surgical/traumatic wound infection, major abscesses, cellulitis, and infected ulcers and burns), in addition to surgical debridement and broad-spectrum antibiotics, empirical therapy for MRSA should be considered pending culture data.\textsuperscript{4}

The IDSA Guideline for Diabetic Foot Infections presents a typical (but not invariable) scenario for the progression of acute infection. Management of diabetic foot infections involves determining the severity of infection as the basis for selecting appropriate treatment. Mild acute superficial cellulitis can probably be treated with agents that only (or predominantly) cover aerobic gram-positive cocci, S. aureus and beta-hemolytic streptococci (groups A, C, and G, but especially group B), in patients who have not recently received antimicrobials while carefully monitoring the response. In the case of chronic infections of moderate severity, it is safest to commence therapy with agents active against gram positive, gram negative, and anaerobic organisms while awaiting culture results. P. aeruginosa should be suspected in an ulcer macerated because of soaking and anaerobes should be suspected if the ulcer is malodorous. The guideline also states: “The pathogenic role of each isolate in a polymicrobial infection is often unclear. ... It is not always necessary to cover all microorganisms isolated from cultures. More virulent species (e.g., S. aureus and group A or B streptococci) should always be covered, but in a polymicrobial infection, less-virulent bacteria (e.g., coagulase-negative staphylococci and enterococci) may be less important. However, if the infection has not responded to the empirical regimen, select agents with activity against all isolates.” Infection in pressure ulcers is usually polymicrobial and may involve exposed deeper structures.\textsuperscript{17}

\textbf{Conclusion}

Tissue biopsy is the gold standard for the culture of wound tissue infection. Scraping the cleaned/debrided wound base with a dermal curette or scalpel blade is an alternative. Attempted aspiration of abscess, bullae, or an area of cellulitis is also optimal.\textsuperscript{2}

These techniques are less likely to collect surface contaminants than is swab collection from the base of a chronic wound and are especially important in serious infection, systemic toxicity, or failure of initial therapy. Nursing home practitioners should become proficient with these techniques or develop systems that provide rapid consultation. Until then, swab culture will be used to determine the resistance pattern of wound pathogens treated in nursing homes and emergency departments.

Whenever possible, systemic antibiotic therapy should be preceded by culture, especially in settings in which MDROs are endemic. Surface organisms contaminate all wounds. Therefore, if the wound is acutely infected and a swab culture is ordered, the wound should be cleaned and irrigated prior to obtaining a specimen from the viable wound bed using the Levine technique.\textsuperscript{7} If the wound requires debridement to produce a clean wound bed, referral to a qualified practitioner should be expedited.\textsuperscript{36} In many
circumstances, debridement/drainage may be more important than antibiotic therapy. The goal is to physically excise dead and unhealthy tissue and to drain abscesses, thereby enabling wound healing by removing a reservoir of potential pathogens. Availability of practitioners capable of performing sharp debridement will also facilitate the collection of specimens following removal of overly devitalized tissue.

Swab cultures should not be used to determine IF the wound is acutely infected; rather, their role may be to identify potential pathogens in a wound judged to be infected based on clinical criteria. Practitioners who utilize swab cultures to guide antibiotic selection for mild infections treated in the nursing home should ensure proper collection technique and be aware that the results may indicate colonization rather than infection (a risk factor for MRSA infection). False-negative results are also a possibility. Antibiotic treatment should be viewed as a therapeutic trial that includes monitoring for deterioration and/or bacteremia. MDRO isolation should heighten the clinician’s level of concern if the prescribed antibiotic did not “cover” the MDRO or other potential pathogens. Deterioration or failure to respond could be related to inadequate debridement of necrotic tissue or abscess, ischemia, inadequate antibiotic penetration, or failure to “cover” the infecting pathogens. We are writing to ask clinicians to consider use of the Levine technique to collect specimens from clinically infected wounds treated in the nursing home, if more invasive sampling is not available or elected. The relative value of “Levine” swab culture versus empiric systemic antibiotic choice on the outcome of mild acute wound infection treated in the nursing home is unknown since neither approach has been tested. The data are meager. Controlled trials are needed. Until then, the issue will remain a “Clinical Controversy.”

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