<u>CANADIAN EMERGENCY DEPARTMENT BEST PRACTICES CHECKLIST FOR</u> <u>SKIN AND SOFT TISSUE INFECTIONS (SSTI): FULL DOCUMENT</u>

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<u>CANADIAN EMERGENCY DEPARTMENT BEST PRACTICES CHECKLIST FOR</u> <u>SKIN AND SOFT TISSUE INFECTIONS (SSTI): FULL DOCUMENT</u> INTRODUCTION

Background: Skin and soft tissue infections (SSTIs) are bacterial infections affecting the skin and underlying tissues.¹ Uncomplicated SSTIs can be non-purulent (i.e., cellulitis or erysipelas) or purulent (i.e., an abscess containing pus). Necrotizing fasciitis is a life-threatening SSTI with involvement of the deeper fascia that carries a mortality rate of 20–30%.² In Canada, cellulitis is the ninth most common reason patients present to an emergency department (ED).³ Given the lack of published data on the impact of purulent SSTIs on Canadian EDs, the burden of SSTIs overall is likely much higher. There are no Canadian guidelines or best practice recommendations for SSTIs. Existing published guidelines in other countries for the diagnosis and management of SSTIs are not practical for use in the ED setting because they were designed for primary care and inpatient settings (and not specific to the ED).⁴⁷ Currently, there are high rates of intravenous (IV) antibiotic use, hospitalization, and treatment failure for SSTIs.⁸⁻¹¹

METHODS

Objective: To adapt existing high-quality SSTI practice guidelines using the CAN-IMPLEMENT^{12,13} process to formulate recommendations for the diagnosis and management of SSTIs specific to the Canadian ED setting.

Scope and Purpose: The Canadian ED Best Practices Checklist for SSTIs provides recommendations for diagnosis, treatment, and disposition of adults with SSTIs specific to the Canadian ED setting. This Checklist covers three conditions: (1) cellulitis; (2) skin abscess; and (3) necrotizing fasciitis. The intended users of this Checklist are Canadian clinicians (attending physicians, residents, nurse practitioners, physician assistants, medical students) working in EDs and urgent care clinics.

What this Checklist Does Not Cover: impetigo, orbital/periorbital cellulitis, perianal abscess, infected mammalian bites, non-bacterial SSTIs (e.g., fungal), diabetic foot infections, infected ulcers, septic arthritis, osteomyelitis, Fournier gangrene, hidradenitis suppurativa, surgical site infections or pediatric patients (age <18 years).

Checklist Format: The recommendations for each condition are presented in three sections (1) Diagnosis; (2) Treatment; and (3) Disposition. Necrotizing fasciitis does not have a disposition section as all patients will require hospital admission. Under each section there is: (1) a key health question; (2) a recommendation; and (3) supporting evidence.

Recommendations: The recommendations are based on the following hierarchy: published highquality guidelines, systematic reviews, and expert opinion. It is made clear with each evidence paragraph if the recommendation was based on:

- (1) Existing guideline recommendation <u>without</u> modification
- (2) Existing guideline recommendation with modification
- (3) High-quality systematic reviews (i.e., a literature search for systematic reviews done when none of the guidelines addressed the key health question)
- (4) Expert opinion (i.e., no guidelines or systematic reviews addressed the key health question). The expert opinion is based on discussion of any existing evidence and the opinions of the Steering Committee.

Stakeholder Involvement: We formed a Steering Committee in January 2023 involving the following key stakeholders: emergency physicians in academic and community sites (N=6), infectious disease physician specialists (N=4), a pharmacist (N=1), patient partners (N=2), and an ED nurse educator (N=1). Methodologic support was provided by implementation scientists, emergency medicine clinician scientists, a PhD biostatistician, and a health sciences librarian.

Key Health Questions: The Steering Committee Chair (KY) drafted a list of Key Health Questions for each target condition. The Steering Committee members all participated in revising the Key Health Questions until there was unanimous agreement. There are 10 key health questions for cellulitis, 10 key health questions for skin abscess, and 4 key health questions for necrotizing fasciitis.

Searching for Guidelines: A health sciences librarian (LS) developed an electronic search strategy to identify existing SSTI guidelines. The search followed guidance provided by PRISMA-Search.¹⁴ The following databases were searched: Medline and Medline in Process via Ovid, Embase Classic, Embase via Ovid, and CINAHL via EBSCOhost. A search strategy was developed in Medline and then translated into the other databases as appropriate (see Appendix A1). The search filter for "Guidelines" was used for all databases to ensure feasibility of the references retrieved. The search was conducted (by LS, KY) to include guidelines published in the past 10 years that would have the most current evidence. The Medline search strategy was peer reviewed by a second health sciences librarian in accordance with the Peer Review of Electronic Search Strategies (PRESS) guideline.¹⁵ All databases were searched from January 1, 2013, to February 7, 2023.

Selecting Guidelines: Two reviewers (KY, DE) independently screened 4,648 abstracts and identified nine guidelines^{4,5,7,16-21} (see Appendix A2 for PRISMA flow diagram). Three Steering Committee members independently appraised all guidelines using the AGREE II instrument²² (see Appendix A3). We included a guideline for adaptation based on a scaled domain score $\geq 60\%$ for the rigor of development domain of the AGREE II instrument (see Appendix A4).

We included five guidelines:

- (1) Practice guidelines for the diagnosis and management of SSTIs by the Infectious Diseases Society of America (IDSA)⁴ - 2014
- (2) Antibiotics after incision and drainage for uncomplicated skin abscesses: a clinical practice guideline (British Medical Journal [BMJ] Rapid Recommendation)¹⁶ 2018
- (3) Clinical guidelines for the antibiotic treatment for community-acquired skin and soft tissue infection (Korean Society of Infectious Diseases)⁵ – 2017
- (4) Cellulitis and erysipelas: antimicrobial prescribing (National Institute for Health and Care Excellence [NICE] Guideline)¹⁷ – 2019
- (5) Optimal timing of initial debridement for necrotizing soft tissue infection: a practice management guideline from the Eastern Association for the Surgery of Trauma (EAST)¹⁸ – 2018

All five guidelines used GRADE (Grading of Recommendations, Assessment, Development and Evaluation) in their development.²³

Recommendation Matrices: The Steering Committee Chair (KY) drafted recommendation matrices. Each matrix was a key health question matched with recommendations (if applicable) from the five guidelines that addressed the question. The recommendations were ordered from highest to lowest quality of evidence determined by the AGREE II Rigor of Domain rating (see Appendix A5 for a sample recommendation matrix).

First Steering Committee Meeting (April 2023): The Steering Committee participated in a twoday virtual meeting in April 2023. There was 100% attendance. A nominal group technique²⁴ was used to ensure all stakeholders provided input. Each stakeholder was given an opportunity to give their views and opinions on each recommendation. The members independently voted on each guideline recommendation (accept without modification, accept with modification, reject). The decision was made with \geq 80% threshold for each vote. If a recommendation was accepted but with modification, the Steering Committee developed the modification, and this was also voted on.

Literature Searches for Systematic Reviews: Six key health questions were not addressed by any guideline. A health sciences librarian (LS) developed six separate electronic search strategies to identify systematic reviews to answer key health questions not addressed by existing guidelines. Medline and Medline in Process via Ovid, and Embase Classic were searched from inception to July 10, 2023 (See Appendix A6 for search strategies).

Selection of Systematic Reviews: The Steering Committee Chair (KY) and a medical student (NS) screened all titles and abstracts followed by full text review of potentially relevant systematic reviews. The quality of the identified systematic reviews was assessed using the AMSTAR-2 tool²⁵ (see Appendix A7). In circumstances where we identified more than one systematic review to answer a key health question, we selected the review with the highest quality.

Conducting a New Systematic Review: one key health question was not addressed by any guideline or systematic review: "Should an anti-inflammatory agent (e.g., non-steroidal anti-inflammatory drug [NSAID], corticosteroid) be prescribed/recommended in addition to antibiotics for cellulitis?" The Steering Committee Chair (KY – senior author) co-led a systematic review to answer this key health question (submitted for publication – revisions sent to journal).

Drafting Recommendations: The Steering Committee Chair (KY) drafted the initial Checklist recommendations for each condition. The Checklist was reviewed for multiple rounds through feedback and discussion with all Steering Committee members via email.

Second Steering Committee Meeting (November 2023): The Steering Committee participated in a two-day hybrid meeting (in-person and virtual) in November 2023. There was 93% attendance on the first day (one member could not attend) and 100% attendance on the second day. We used a nominal group technique²⁴ to ensure all stakeholders provided input. Each key health question, recommendation and accompanying evidence was reviewed. The final content of the Checklist was accepted by group consensus.

Final Checklist Review: Non-Steering Committee members reviewed the SSTI Best Practices Checklist: two implementation scientists, four emergency medicine clinician scientists, and a PhD biostatistician. The Checklist was reviewed by the Chair of the Canadian Association of Emergency Physicians (CAEP) Standards Subcommittee and then posted online for CAEP member review for 30 days. All input was considered when drafting the final Checklist.

Endorsement: The Checklist is endorsed by CAEP. The study protocol was endorsed by the Network of Canadian Emergency Researchers.

Funding: This project was funded by a 2023 PSI Graham Farquharson Knowledge Translation Fellowship award and an Ottawa Hospital Research Institute ELEVATE Seed Funding Grant. The views of these funding bodies did not influence the content of the Checklist.

Competing Interests: One Steering Committee member (RZ) participated as part of a scientific planning committee for the management of SSTIs funded by Paladin Labs. None of the other co-authors have any competing interests to declare.

Acknowledgments: We would like to thank: Dr. Stuart Nicholls (patient engagement specialist) for his assistance connecting with patient partners for this project; Dr. Shawn Mondoux (CAEP Standards Subcommittee Chair) for external review; Ms. Carolyne Kennedy and Ms. Catherine Clement for administrative support; and the Network of Canadian Emergency Researchers for study protocol review, feedback and endorsement.

NON-PURULENT CELLULITIS

DIAGNOSIS

Q1. How should cellulitis be diagnosed in the emergency department (ED)? <u>Recommendation</u>:

- (1) Use clinical judgment to diagnose cellulitis. Typical physical exam findings suggestive of cellulitis are tenderness, erythema, increased warmth, edema, and induration. On occasion, there may be lymphangitis and/or fever.
- (2) Do not use existing decision tools or specific investigations (e.g., white blood cell count, C-reactive protein) to diagnose cellulitis. Consider an alternative diagnosis in patients with bilateral symptoms (e.g., involvement of both legs).

<u>Evidence</u>: This recommendation is based on evidence from a systematic review. This key health question was not addressed by any of the included guidelines. We conducted a literature search and identified one systematic review by Patel et al.²⁶, which examined diagnostic criteria for lower limb cellulitis. This study included 8 observational studies, which examined the utility of biomarkers (N=5), imaging (N=2) and a clinical decision tool (N=1) to diagnose cellulitis. All included studies had a high risk of bias in at least one domain. Ultimately, this review found that there is insufficient evidence to support any diagnostic criteria or tools for lower limb cellulitis. We did not identify any high-quality reviews for cellulitis at other anatomical sites.

Q2. Should blood cultures be ordered for patients with cellulitis?

Recommendation: Do not routinely order blood cultures for systemically well patients with cellulitis.

Consider ordering blood cultures in patients with cellulitis who are:

- (1) systemically unwell (e.g., fever, lymphangitis, persistent tachycardia, tachypnea, hypotension); or
- (2) immunosuppressed (e.g., active malignancy receiving anticancer therapy, known or suspected neutropenia)

<u>Evidence</u>: This recommendation is based on modification of existing guideline recommendations. The Steering Committee accepted the IDSA⁴ and Korean⁵ guideline recommendations but with modifications. We discussed that given the low yield (typically <5%)^{27,28} for blood cultures in patients with cellulitis, blood cultures should not be routinely ordered for <u>systemically well</u> patients. Both guidelines discussed use of cutaneous aspirates, biopsies, or swabs in addition to blood cultures when making recommendations. The Steering Committee chose to remove mention of aspirates, biopsies, and swabs, as we felt these tests had no role in the assessment of ED patients with cellulitis. Both guidelines listed immunosuppression, neutropenia and receiving anticancer therapy as separate indications for blood cultures. For clarity, the Steering Committee opted to list receiving anticancer therapy and neutropenia as examples of immunosuppression.

Q3. Should ED clinicians order imaging for cellulitis?

<u>Recommendation</u>: Do not routinely order imaging for cellulitis. Perform bedside point-of-care ultrasound (POCUS) in cases where there is uncertainty in differentiating skin abscess from cellulitis.

Consider ordering imaging (e.g., X-ray, computed tomography [CT], ultrasound) in select cases:

- (1) suspected osteomyelitis
- (2) foreign bodies
- (3) uncertainty in differentiating from necrotizing fasciitis (note: imaging should never delay urgent surgical consultation if there is clinical suspicion).

<u>Evidence</u>: This recommendation is based on modification of an existing guideline recommendation. The Steering Committee accepted the Korean guideline⁵ recommendation with modifications to suggest <u>imaging (e.g., X-ray, CT, ultrasound)</u> instead of CT alone as some EDs may not have access to one or more imaging modalities. <u>Foreign bodies</u> were added as an indication to consider imaging. The term <u>uncertainty</u> in differentiating from necrotizing fasciitis was added, but with the caveat that this should never delay urgent surgical consultation if there is clinical suspicion. The recommendation to use POCUS is based on evidence from a meta-analysis by Gottlieb et al²⁹, which showed that POCUS had a high diagnostic accuracy for evaluation of skin abscesses in adults: sensitivity 98.7%, specificity 91.0%. The authors reported use of POCUS led to a correct change in management for 10.3% of cases, and an incorrect change in management in 0.7% of cases.

TREATMENT

Q4. What is the recommended oral antibiotic (i) agent (ii) dose (iii) frequency and (iv) duration to treat cellulitis?

Recommendation: Oral antibiotics are first line treatment. Please refer to Table 1.

<u>Evidence</u>: This recommendation is based on modification of existing guideline recommendations. All antibiotic treatment regimens were developed by the Steering Committee by reviewing existing guideline treatment recommendations and then adapting them specifically to the Canadian ED context. The Steering Committee members felt it was important to include patient factors useful to ED clinicians such as allergy, pregnancy, breastfeeding, and kidney impairment.

Q5. When should the ED clinician consider intravenous (IV) antibiotics to treat cellulitis? <u>Recommendation:</u> Treat with IV antibiotics in the following patients:

- (1) systemically unwell (e.g., fever, lymphangitis, persistent tachycardia, tachypnea, hypotension); or
- (2) failed oral antibiotic treatment (new/persistent fever, worsening pain, and/or spreading erythema despite at least 48-72 hours of oral antibiotics); or
- (3) cannot tolerate oral intake (e.g., vomiting, malabsorption syndrome, etc.)

<u>Evidence</u>: This recommendation is based on modification of an existing IDSA guideline⁴ recommendation. We added criteria for treatment failure and those that <u>cannot tolerate oral intake</u> was added as an indication.

Q6. If IV antibiotics are started, what is the recommended antibiotic (i) agent (ii) dose (iii) frequency and (iv) duration to treat cellulitis?

Recommendation: Please refer to Table 1. See answer to Q4 for evidence.

Q7. Is elevation of the affected area recommended?

<u>Recommendation</u>: Advise patients with limb cellulitis to elevate the affected area as this will hasten improvement by promoting gravity drainage of edema and inflammatory substances.

Evidence: This recommendation is based on an existing guideline (IDSA⁴) recommendation without modification.

Q8. Should an anti-inflammatory agent (e.g., non-steroidal anti-inflammatory drug [NSAID], corticosteroid) be prescribed/recommended in addition to antibiotics for cellulitis?

<u>Recommendation</u>: Consider recommending or prescribing an oral NSAID for 5 - 7 days (if no contraindications) as an adjunct to antibiotic treatment in patients with cellulitis.

<u>Evidence</u>: This recommendation is based on evidence from a systematic review. The IDSA guideline recommendation states 'systemic corticosteroids (e.g., prednisone 40 mg daily for 7 days) could be considered in nondiabetic adult patients with cellulitis' – weak recommendation, moderate quality evidence.⁴ This was based on a single RCT in 1997 that included 112 inpatients randomized to a prednisolone taper or placebo.³⁰ The Steering Committee felt more evidence was required to answer this question. The Steering Committee Chair (KY) co-led a systematic review and meta-analysis^[ref], which identified 5 RCTs (N=331 participants) comparing an anti-inflammatory (corticosteroid or NSAID) to either placebo or no intervention as adjunct cellulitis treatment. For clinical response, there was a benefit with an oral NSAID (no data for corticosteroids) at day 3 (RR 1.81, 95%CI 1.42 – 2.31). There was no difference between groups for clinical cure up to 22 days. Given the best available evidence but acknowledging the small number of studies, the Steering Committee opted to recommend <u>considering</u> an oral NSAID, as this may improve early clinical response.

DISPOSITION

Q9. Which ED patients with cellulitis should be considered for hospital admission?

Recommendation: Consider hospital admission in patients with any of the following:

- (1) challenges with adherence to therapy
- (2) immunosuppressed (e.g., active malignancy receiving anticancer therapy, known or suspected neutropenia)
- (3) failed outpatient antibiotic treatment (i.e., new/persistent fever, worsening pain, and/or spreading erythema despite at least 48-72 hours of antibiotic therapy)
- (4) systemically unwell (e.g., fever, lymphangitis, persistent tachycardia, tachypnea, hypotension)

<u>Evidence</u>: This recommendation is based on modification of an existing guideline recommendation. The IDSA guideline⁴ recommendation was accepted with modification. The criterion 'severely immunocompromised' was changed to <u>immunosuppressed</u> (with examples) as the Steering Committee felt this was clearer. The Steering Committee opted to add <u>systemically unwell</u> (with examples) as a criterion for considering hospital admission. The criterion 'concern for a deeper or necrotizing infection' was removed as the current key health question is based on a diagnosis of cellulitis having been made. In cases where there is concern for a necrotizing infection, separate recommendations are available (see SSTI Best Practices Checklist for Necrotizing Fasciitis).

Q10. When should patients with cellulitis be reassessed by a healthcare provider?

<u>Recommendation</u>: Advise patients to see a healthcare provider 72 hours after antibiotic treatment is started if there is no improvement. Instruct patients to return to the ED before 72 hours if they develop severe pain out of proportion or rapidly spreading painful erythema.

<u>Evidence</u>: This recommendation is based on evidence from a systematic review and expert opinion. The NICE guideline¹⁷ discussed reassessing patients with cellulitis within 2-3 days for those that do not improve as an expert opinion. We conducted a literature search and identified a systematic review and meta-analysis by Yadav et al.³¹, which examined the impact of antibiotics on clinical response over time for uncomplicated cellulitis (32 RCTs, N=13,576 participants). Time to improvement was: 5 days for 50% reduction of pain, 2–3 days for 33% reduction in erythema, and 2-4 days for a 30–50% reduction in edema. While the data must be interpreted with caution due to considerable heterogeneity and small number of included studies, the best available data suggest the

optimal time to clinical reassessment is between 2–4 days. The Steering Committee felt that reassessment at 48 hours may be too soon to observe appropriate clinical response, which may lead to premature escalation or change in antibiotic treatment. Given this concern, we recommend 72 hours as the timepoint at which patients should be reassessed by a healthcare provider if having no improvement. As an expert opinion, we recommend patients should return to the ED before 72 hours if developing pain out of proportion or rapidly spreading painful erythema, which would be worrisome for a potential necrotizing infection.

Table 1. Antibiotic Treatment Recommendations for Non-Purulent Cellulitis

Non-purulent Cellulitis

| Antibiotic dur | ntibiotic duration: 5–7 days* | | |
|---|--|--|--|
| | Recommended Regimens** | Notes | |
| Oral options | Cephalexin 500–1000 mg Q6H Cefadroxil 500–1000 mg Q12H Cloxacillin 500–1000 mg Q6H [†] | First-line options (unless known or suspected MRSA). | |
| | Penicillin V 300–600 mg Q6H [†] Amoxicillin 500–1000 mg Q8H | Penicillin and amoxicillin are indicated for mild erysipelas only. Erysipelas is a superficial skin infection with clear demarcation of involved skin. | |
| | Trimethoprim-sulfamethoxazole 1 or 2 double strength tablets Q12H Clindamycin 300–450 mg Q6–8H Doxycycline 100 mg Q12H [‡] | These agents may be associated with higher antibiotic resistance rates, lower efficacy and/or a greater risk of adverse effects than the options above. | |
| | Moxifloxacin 400 mg daily or Levofloxacin 500 mg daily | Reserve for patients with severe (e.g., IgE-mediated) allergy or contraindications to penicillins and cephalosporins. | |
| IV options | Cefazolin 1–2 g Q8H | First-line option (unless known/suspected MRSA [®]). | |
| | Ceftriaxone 1–2 g Q24H | Ceftriaxone has less reliable activity for <i>Staphylococcus aureus</i> compared to Streptococcus sp. | |
| | Vancomycin 15 mg/kg Q8–12H Clindamycin 600 mg Q8H | Reserve for patients with contraindications to cephalosporin options above. | |
| *Consider 5 days duration for infections that are of mild severity. | | | |

** Higher dose in range may be used for more severe infections, obese patients (e.g., BMI ≥30). Caution: increased risk of GI side effects with larger oral doses.

[†]Should be taken on an empty stomach.

[‡]Administer with a full glass of water; patient should stay upright (not lie down) for 1 to 2 hours after administration. May be taken with food to minimize GI upset.

| Special Populations | | | |
|---------------------|---|--|--|
| Penicillin allergy | AVOID penicillin, amoxicillin and cloxacillin. AOVID cephalexin and cefadroxil in patients with severe | | |
| | (e.g., IgE-mediated) allergy to penicillin. Risk of allergic reaction to cefazolin or ceftriaxone in patients | | |
| | with penicillin allergy is low (1-2%). AVOID β -lactams if history of a severe cutaneous reaction (e.g., | | |
| | Stevens-Johnson Syndrome [SJS], drug reaction with eosinophilia and systematic symptoms [DRESS]). | | |
| Cephalosporin | Cefazolin may be considered if cephalosporin allergy (e.g., cephalexin, ceftriaxone) was non-severe and | | |
| allergy | not to cefazolin. | | |
| | Ceftriaxone may be considered if cephalosporin allergy was non-severe and not to ceftriaxone, | | |
| | cefotaxime, cefepime, or cefuroxime. | | |
| Pregnancy | Penicillins, cephalosporins, trimethoprim-sulfamethoxazole in 2 nd & 3 rd trimester (avoid in 1 st trimester | | |
| | and near term) and vancomycin are considered safe in pregnancy; clindamycin may be considered if | | |
| | necessary. | | |
| | AVOID doxycycline and fluoroquinolones (e.g., moxifloxacin/levofloxacin). | | |
| Breastfeeding | Penicillins, cephalosporins, doxycycline and vancomycin are considered compatible with breastfeeding. | | |
| | Trimethoprim-sulfamethoxazole is compatible in older (> 2 months), healthy, full-term infants who are | | |
| | not G6PD deficient. Clindamycin may be considered if necessary. Infant should be monitored for rash, | | |
| | diarrhea, thrush, etc. AVOID fluoroquinolones (e.g., moxifloxacin/levofloxacin). | | |
| Kidney | Amoxicillin, cephalexin, cefadroxil, cefazolin, levofloxacin, penicillin V, trimethoprim-sulfamethoxazole | | |
| impairment | and vancomycin REQUIRE dose adjustment. Increased risk of hyperkalemia with trimethoprim- | | |
| | sulfamethoxazole; caution with concomitant use of medications that increase serum potassium. | | |

| (CrCl < 30–50 | Cloxacillin, ceftriaxone, clindamycin, doxycycline and moxifloxacin do NOT require dose adjustment. | |
|--|---|---------------------------|
| mL/min) | | |
| Known or | Oral options: | IV Options: |
| suspected | Trimethoprim-sulfamethoxazole, Clindamycin or | Vancomycin or Clindamycin |
| MRSA§ | Doxycycline | |
| [§] NOTE: most cases of non-purulent cellulitis are due to streptococci and should be treated with a β-lactam antibiotic. Suspect | | |
| MRSA if: known MRSA colonization, prior MRSA infection, high-risk group (e.g., injection drug use, homeless in the last | | |
| year, crowded living conditions, correctional facility), or failed adequate course of β -lactam therapy. | | |

UNCOMPLICATED PURULENT SSTI (SKIN ABSCESS)

DIAGNOSIS

Q1. How should skin abscesses be diagnosed in the ED?

<u>Recommendation</u>: Use clinical judgment to diagnose a skin abscess. Typical physical exam findings are like non-purulent cellulitis (pain, erythema, increased warmth, edema, and induration) plus a palpable area of fluctuance that may represent an underlying purulent collection).

In cases where there is uncertainty about an underlying collection on physical exam, use point of care ultrasound (POCUS) as an adjunct (see Q2).

<u>Evidence</u>: This recommendation is an expert opinion. None of the included guidelines addressed the question of how a skin abscess should be diagnosed. We conducted a literature search of systematic reviews and identified a study by Patel et al.²⁶ that addressed diagnosis of cellulitis, but no data were available for skin abscess. The Steering Committee decided that given the lack of available evidence, the emphasis should be on clinical diagnosis of skin abscess while highlighting key physical exam features unique to skin abscess (palpable area of fluctuance).

Q2. For ED patients with suspected uncomplicated abscesses, when should point of care ultrasound (POCUS) be used?

<u>Recommendation</u>: Use POCUS in all cases where there is uncertainty in differentiating skin abscess from cellulitis. POCUS will identify the presence of an underlying collection in patients with a skin abscess.

<u>Evidence</u>: This recommendation is based on evidence from a systematic review. The potential role of POCUS was not addressed in any of the included guidelines. Following a literature search, we identified five abstracts. On full text review, one article was removed (conference abstract with no full manuscript published). The four remaining systematic reviews were assessed using AMSTAR-2.²⁵ Following this, a systematic review and meta-analysis by Gottlieb et al.²⁹ was chosen as the highest quality of evidence to answer this key health question. This systematic review included 14 studies (N=2,656 participants), of which 13 studies were conducted in the ED setting. All studies were observational (13 prospective, 1 retrospective). POCUS had a high diagnostic accuracy for evaluation of skin abscesses, particularly in adults: sensitivity 98.7%, specificity 91.0%, positive likelihood ratio 10.9, negative likelihood ratio 0.01. The authors reported use of POCUS led to a correct change in management for 10.3% of cases, and an incorrect change in management in 0.7% of cases. Based on this evidence, the Steering Committee recommended the use of bedside POCUS in all cases where there is uncertainty differentiating skin abscess from cellulitis.

Q3. Should blood cultures be ordered for patients with skin abscesses?

<u>Recommendation</u>: Do not routinely order blood cultures for patients with a skin abscess.

Consider ordering blood cultures in patients with skin abscess who are:

- (1) systemically unwell (e.g., fever, lymphangitis, persistent tachycardia, tachypnea, hypotension)
- (2) immunosuppressed (e.g., active malignancy receiving anticancer therapy, known or suspected neutropenia)

<u>Evidence</u>: This recommendation is an expert opinion. While included guidelines recommended against routinely ordering blood cultures for patients with cellulitis, they did not separately address this question for skin abscesses. We conducted a literature search and did not identify any systematic

reviews about the utility of blood cultures in patients with skin abscess. The Steering Committee discussed that given the low yield (typically <5%)^{27,28} for blood cultures in patients with cellulitis, there was no evidence to suggest that the yield would be any higher for patients with skin abscess. Thus, we recommend that blood cultures should not be routinely ordered but may be considered in patients who are systemically unwell or immunosuppressed.

TREATMENT

Q4. What is the recommended bedside treatment for uncomplicated skin abscesses? <u>Recommendation</u>: Perform a bedside incision and drainage (I&D) for abscesses. Do not perform needle aspiration.

<u>Evidence</u>: This recommendation for I&D is based on an existing guideline recommendation (IDSA⁴) with modification. We removed mention of <u>inflamed epidermoid cysts</u>, <u>carbuncles</u>, <u>and</u> <u>large furuncles</u> for simplicity. We added a recommendation not to perform needle aspiration based on a randomized controlled trial (RCT) that showed overall success with ultrasound-guided needle aspiration was 26% (95%CI 18% to 44%) compared to 80% (95%CI 66% to 89%) for I&D.³²

Q5. Following incision and drainage (I&D) of a skin abscess, should the abscess cavity be packed with packing material?

Recommendation: Do not routinely pack skin abscess cavities following bedside I&D.

Evidence: This recommendation is based on evidence from a systematic review. The IDSA guideline states "some clinicians close the wound with sutures or pack it with gauze or other absorbent material. One small study, however, found that packing caused more pain and did not improve healing when compared to just covering the incision site with sterile gauze".⁴ This was not an explicit guideline recommendation and this key health question was not addressed by any of the other included guidelines. We conducted a literature search and identified two abstracts – one study was excluded because it was a conference abstract without the full manuscript being published. We included a systematic review and meta-analysis by Mohamedahmed et al.³³, which included 8 RCTs (N=485 participants). Three RCTs assessed anorectal abscesses only, whereas five RCTs included abscesses at various anatomical sites. Oral antibiotics were routinely given in four RCTs, selectively given in one RCT, not given in one RCT, and it was unclear if antibiotics were given in the remaining two RCTs. There was no difference in risk of recurrence for packing versus no packing (relative risk 1.31, P=0.56). The included trials had small sample sizes which limit the strength of conclusions that can be drawn. However, this study is the best available evidence that demonstrates comparable outcomes between groups. Given no strong evidence to favour packing of abscess cavities, the Steering Committee agreed with the authors' suggestion that no packing may be more favourable given the pain patients experience.³⁴

Q6. Following I&D of a skin abscess, when should antibiotics be prescribed?

<u>Recommendation</u>: Prescribe antibiotics as an adjunct to I&D in cases of extensive cellulitis near the purulent lesion or in patients with systemic symptoms such as fever. Consider antibiotics for patients that are immunosuppressed (e.g., active malignancy receiving anticancer therapy, known or suspected neutropenia).

<u>Evidence</u>: This recommendation is based on modification of existing guideline recommendations. The Steering Committee accepted both the Korean⁵ and IDSA⁴ guideline recommendations with modifications. The present statement was modified to emphasize that use of antibiotics is an <u>adjunct</u> to I&D. The Steering Committee favoured the Korean guideline suggestion of recommending antibiotics in patients with systemic symptoms such as fever instead of the IDSA guideline recommendation which suggested use of antibiotics in patients with "systemic inflammatory response syndrome (SIRS)".

Q7. If an oral antibiotic is prescribed for a patient with a skin abscess, what oral antibiotic (i) agent (ii) dose (iii) frequency and (iv) duration is recommended?

Recommendation: Please refer to Table 2. If antibiotics are prescribed, oral antibiotics are first line.

<u>Evidence</u>: This recommendation is based on modification of existing guideline recommendations. All antibiotic treatment regimens were developed by the Steering Committee by reviewing existing guideline treatment recommendations and then adapting them specifically to the Canadian ED context. The Steering Committee members felt it was important to include patient factors useful to ED clinicians such as methicillin resistant *Staphylococcus aureus* (MRSA) risk factors, allergy, pregnancy, breastfeeding, and kidney impairment.

Q8. For patients with skin abscess, when should the ED clinician treat with intravenous (IV) antibiotics?

Administer IV antibiotics for patients for whom antibiotics are indicated but who:

- have had treatment failure following I&D plus appropriate oral antibiotics (treatment failure defined as new/persistent fever, worsening pain, and/or spreading erythema despite at least 48-72 hours of oral antibiotics); or
- (2) are systemically unwell (e.g., fever, lymphangitis, persistent tachycardia, tachypnea, hypotension); or
- (3) cannot tolerate oral intake (e.g., vomiting, malabsorption syndrome, etc.)

<u>Evidence</u>: This recommendation is based on modification of an existing guideline recommendation. The Steering Committee accepted the IDSA guideline⁴ recommendation with modifications. We wished to emphasize that IV antibiotics should be considered in those that have failed <u>to improve</u> <u>following</u> I&D plus <u>appropriate</u> oral antibiotics. The Steering Committee opted to use the term <u>systemically unwell</u> (with examples) instead of SIRS criteria and added <u>cannot tolerate oral intake</u> (with examples) as an additional criterion for requiring IV antibiotics.

Q9. If an IV antibiotic is started for a patient with a skin abscess, what IV antibiotic (i) agent (ii) dose (iii) frequency and (iv) duration is recommended?

Recommendation: Please refer to Table 2. See answer to Q7 for evidence.

DISPOSITION

Q10. When should patients with skin abscess be reassessed by a healthcare provider? <u>Recommendation</u>: Advise patients to see a healthcare provider 72 hours after I&D is performed if there is no improvement, recurrence, or worsening of symptoms.

<u>Evidence</u>: This recommendation is an expert opinion. None of the included guidelines addressed this key health question. Following a literature search, a systematic review and meta-analysis by Yadav et al.³¹ was identified, which suggested the optimal time to clinical reassessment for cellulitis was between 2 - 4 days. However, this review excluded patients with skin abscesses and no other reviews addressed time to reassessment specifically for skin abscesses. The Steering Committee felt

that recommending a similar timeframe to reassessment for patients with skin abscesses as for cellulitis (i.e., at 3 days) was reasonable.

Table 2. Antibiotic Treatment Recommendations for Purulent Cellulitis (Skin Abscess)

| Purulent Cellulitis (i.e., Skin Abscess) | | | | |
|---|--|--|--|--|
| | | | | |
| If antibiotic therapy required after incision and drainage | | | | |
| Antibiotic duratio | n: 7–10 days | | | |
| | Recommended Regimens* | Notes | | |
| | | | | |
| | | | | |
| | Cephalexin 500–1000 mg Q6H Cefadroxil 500–1000 mg Q12H | First-line options (unless known or suspected MRSA®) | | |
| | Cloxacillin 500–1000 mg QoH | | | |
| Oral options | Trimethoprim-sulfamethoxazole 1 or 2 double strength tablets Q12H Clindamycin 300–450 mg Q6-8H | These agents may be associated with higher antibiotic resistance rates, lower efficacy and/or higher adverse effects than the options above. | | |
| | Doxycycline 100 mg Q12H [‡] Moxifloxacin 400 mg daily or levofloxacin 500 mg daily | Reserve for patients with severe (e.g., IgE-mediated) allergy or contraindications to penicillins and cephalosporins. | | |
| | Cefazolin 1–2 g Q8H | First-line option (unless known or suspected MRSA [®]). | | |
| IV options | Ceftriaxone 1–2 g Q24H | Ceftriaxone has less reliable activity for <i>Staphylococcus aureus</i> compared to Streptococcus sp. | | |
| | Vancomycin 15 mg/kg Q8–12H Clindamycin 600 mg Q8H | Reserve for patients with contraindications to cefazolin. | | |
| | | | | |
| *Higher dose in range may be used for more severe infections, obese patients (e.g., BMI ≥30); caution increased risk of GI side effects with larger oral doses. †Should be taken on an empty stomach. ‡Administer with a full glass of water; patient should stay upright (not lie down) for 1 to 2 hours after administration. May be taken with food to minimize GI upset. Some clinicians may add a β-lactam agent (e.g., penicillin, amoxicillin, cephalexin) to doxycycline for improved Streptococcus coverage. | | | | |
| Special Population | ns | | | |
| Known or | Oral options: | IV Options: | | |
| suspected MRSA [®] | I rimethoprim-sulfamethoxazole, Clindamycii | n Vancomycin or Clindamycin | | |
| Suspect MRSA if: | or Doxycycline | on high risk group (e.g. injection drug use homeless in the last | | |
| vear crowded living | a conditions correctional facility) or failed adeo | use course of B-lactam therapy | | |
| Penicillin allergy | AVOID cloxacillin. AVOID cephalexin and c | refadroxil in patients with severe (e.g. IgE-mediated) allergy to | | |
| r enternin (merg) | penicillin. Risk of allervic reaction to cefazolin or ceftriaxone in patients with penicillin allerov is low (1-2%) | | | |
| | AVOID B-lactams if history of a severe cutaneous reaction (e.g. Stevens -Johnson Syndrome ISIS) drug | | | |
| | reaction with eosinophilia and systematic symptoms [DRESS]). | | | |
| Cephalosporin | Cefazolin may be considered if cephalosporin | allergy (e.g., cephalexin, ceftriaxone) was non-severe and not to | | |
| allergy | cefazolin. Ceftriaxone may be considered if cephalosporin allergy was non-severe and not to ceftriaxone, | | | |
| | cefotaxime, cefepime, or cefuroxime. | | | |
| Pregnancy | Penicillins, cephalosporins, trimethoprim-sulfamethoxazole in 2 nd & 3 rd trimester (avoid in 1 st trimester and | | | |
| | near term) and vancomycin are considered safe in pregnancy; clindamycin may be considered if necessary. AVOID doxycycline and fluoroquinolones (e.g., moxifloxacin/levofloxacin). | | | |
| Breastfeeding | Penicillins, cephalosporins, doxycycline and vancomycin are considered compatible with breastfeeding. | | | |
| | Trimethoprim-sulfamethoxazole is compatible in older (> 2 months), healthy, full-term infants who are not | | | |
| | G6PD deficient. Clindamycin may be conside | red it necessary. Infant should be monitored for rash, diarrhea, | | |
| | thrush, etc. AVOID fluoroquinolones (e.g., r | noxitioxacin/levofloxacin). | | |

| Kidney | Cephalexin, cefadroxil, cefazolin, levofloxacin, trimethoprim-sulfamethoxazole, and vancomycin REQUIRE |
|------------------|--|
| impairment | dose adjustment. Increased risk of hyperkalemia with trimethoprim-sulfamethoxazole; caution with |
| (CrCl < 30 - 50) | concomitant use of medications that increase serum potassium. |
| mL/min) | Cloxacillin, ceftriaxone, clindamycin, doxycycline, and moxifloxacin do NOT require dose adjustment. |

COMPLICATED SSTI (NECROTIZING FASCIITIS)

DIAGNOSIS

Q1. When should the ED physician suspect a diagnosis of necrotizing fasciitis?

<u>Recommendation</u>: Use clinical judgment to decide if necrotizing fasciitis should be suspected. Suspect necrotizing fasciitis if a patient presents with features that suggest involvement of deeper tissues such as:

- (1) Severe pain that seems disproportional to the clinical findings.
- (2) The hard, wooden feel of the subcutaneous tissue, extending beyond the area of apparent skin involvement.
- (3) Systemic toxicity, often with altered mental status.
- (4) Edema or tenderness extending beyond the cutaneous erythema.
- (5) Crepitus, indicating gas in the tissues.
- (6) Bullous lesions.
- (7) Skin necrosis or ecchymoses.

<u>Evidence</u>: This recommendation is based on modification of an existing guideline recommendation. The Steering Committee accepted the IDSA guideline⁴ recommendation but with modification. Specifically, 'failure to respond to initial antibiotic therapy' was removed as a feature that may suggest involvement of deeper tissues.

Q2. Is there a role for radiologic investigations (e.g., X-ray, ultrasound, computed tomography [CT] or magnetic resonance imaging [MRI]) in the ED evaluation of necrotizing fasciitis?

<u>Recommendation</u>: Do not rely on imaging tests to help diagnose necrotizing fasciitis. Instead, use clinical judgment to help make the diagnosis. Imaging and blood tests should not delay urgent surgical consultation for patients with a high clinical suspicion, as definitive diagnosis is made in the operating room.

<u>Evidence</u>: This recommendation is based on evidence from a systematic review. The Steering Committee rejected the IDSA and Korean guideline statements about the potential role of radiologic investigations in diagnosing necrotizing fasciitis. Instead, a literature search for systematic reviews was undertaken to answer this question. A systematic review and meta-analysis by Fernando et al.³⁵ highlighted that plain x-ray is poorly sensitive for the diagnosis of necrotizing fasciitis. Whereas CT has superior sensitivity and specificity compared to plain X-ray, the authors of this review highlighted that even if available, CT imaging may delay definitive surgical diagnosis and management. MRI was not recommended based on lack of availability and risk of significant delay to surgical intervention. The Steering Committee felt it was important to emphasize the importance of clinical judgment so as not to delay urgent surgical consultation.

Q3. Is there a role for laboratory investigations in the ED evaluation of necrotizing fasciitis? <u>Recommendation</u>:

- (1) Obtain wound cultures (if appropriate) from infected tissue or abscess samples to help identify causative bacteria.
- (2) Order blood cultures as they are helpful to identify causative bacteria.
- (3) Do not use decision tools, such as the Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score, to rule out the diagnosis. The LRINEC score is poorly sensitive for the diagnosis of necrotizing fasciitis.

Evidence: This recommendation is based on modification of an existing guideline recommendation and evidence from a systematic review. For the role of lab tests in the diagnosis of necrotizing fasciitis, the Steering Committee accepted the Korean guideline⁵ with modifications. We emphasized the importance of wound cultures (if appropriate) and blood cultures for identification of causative bacteria, which could help tailor downstream antibiotic treatment. With respect to the LRINEC score (which consists of six blood test laboratory values), in the aforementioned meta-analysis by Fernando et al.³⁵, the LRINEC score had poor sensitivity (using a cut-off score of \geq 6, sensitivity = 68.2%, using a cut-off score of \geq 8, sensitivity = 40.8%) for the diagnosis of necrotizing fasciitis.

TREATMENT

Q4. What is the appropriate initial ED management for patients with suspected necrotizing fasciitis?

Recommendation:

- (1) Request immediate surgical consultation.
- (2) Order intravenous (IV) antibiotic therapy (see Table 3). Do not delay antibiotic therapy while waiting for ancillary investigations or consultations.
- (3) Order cardiac monitoring, analgesia, IV fluid resuscitation and vasopressors if required for ongoing hemodynamic instability.

<u>Evidence</u>: This recommendation is based on modification of an existing guideline recommendation. The Steering Committee accepted the IDSA guideline⁴ recommendation about early surgical consultation with minor modification. We emphasized the need for <u>immediate</u> surgical consultation. For treatment recommendations, the Steering Committee reviewed all included guidelines for antibiotic treatment of necrotizing fascilitis and then drafted antibiotic treatment recommendations specific to the Canadian ED context (see Table 3).

Table 3. Antibiotic Treatment Recommendations for Necrotizing Fasciitis

Necrotizing Fasciitis

| | Recommended Regimen | Notes |
|--|--|--|
| | | |
| First Line | Piperacillin-tazobactam 4.5 g IV Q6H AND Clindamycin 900 mg IV Q8H AND Vancomycin 20–25 mg/kg IV loading dose | Subsequent doses of vancomycin (Q8-12H) are based on weight and kidney function. |
| Second Line | Carbapenem (e.g., ertapenem 1 g IV Q24H, meropenem 1 g IV Q8H, or imipenem 500 mg IV Q6H) AND | Use a carbapenem for patients with allergy to penicillin. |
| | Clindamycin 900 mg IV Q8H AND Vancomycin 20–25 mg/kg IV loading dose | Subsequent doses of vancomycin (Q8-12H) are based on weight and kidney function. |
| Special Populations | | |
| Penicillin allergy | Use second line regimen; low risk of cross-allergy with carbapenems and penicillins. | |
| Pregnancy | Penicillins and vancomycin are considered safe in pregnancy. Limited data for carbapenems but generally considered safe; meropenem/ertapenem may be preferred over imipenem. The benefits of clindamycin for suspected necrotizing infections outweigh any risks and should be administered. | |
| Kidney impairment (CrCl < 30-50 mL/min) | For suspected necrotizing infections, do NOT adjust initial doses for patients with kidney impairment. Piperacillin, carbapenems and vancomycin REQUIRE dose adjustment (for subsequent doses). Clindamycin does NOT require dose adjustment. | |

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