Erysipelas and Cellulitis in Adults - Microbiology Full Clinical Guideline

Reference number:CG-ANTI/2016/008

Introduction

- If skin colonisation with beta-haemolytic streptococci or *Staphylococcus aureus* coincides with skin breach, these bacteria can invade the soft tissues.
- Bacterial invasion of the dermis and superficial subcutis – with acute presentation and clear demarcation of infected and uninfected tissue – is termed erysipelas.
- Bacterial invasion of the dermis and subcutis – varying from erysipelas with its relatively indolent presentation and without the sharp division of infected and uninfected tissue – is termed cellulitis.
- The commonest causes of erysipelas and cellulitis are the beta-haemolytic streptococci:
    - Of the groups A, B, C, and G, *Streptococcus* groups A and G are responsible for the majority of infectious episodes.
- *Staphylococcus aureus* - methicillin susceptible or resistant *Staphylococcus aureus* (MSSA or MRSA) - is another relatively common bacterial cause.
- Breaches in the skin can be secondary to:
    - Trauma: e.g. insect bites, injections of intravenous drug usage, penetrating injuries, pressure ulceration, vascular ulceration.
    - Inflammation: e.g. eczema, psoriasis.
    - Infection: e.g. impetigo, tinea pedis, varicella.
- Symptoms and signs of erysipelas/cellulitis include skin erythema, warmth, and oedema.
- Temperatures > 38 ° C or < 36 ° C, respiratory rate > 20 breaths/minute, heart rate > 90 beats/minute, and hypotension can denote progression of localised infectious disease into sepsis and septic shock.
- NB Please note that skin infections can be associated with varying reservoirs, mechanisms of transmission, locations of infection, and past medical histories:
    - Specific local guidance exists for: necrotising soft tissue infections; orbital/postseptal cellulitis; periorbital/preseptal cellulitis; soft tissue infection associated with water exposure; superficial, soft tissue infection associated with cat or dog bites; superficial, soft tissue infection associated with human bites; superficial, soft tissue infection associated with insect bites or bee/hornet/wasp stings; and superficial, soft tissue infection associated with lacerations.
    - Please also note that specific national guidance exists for cellulitis in lymphoedema: Guidelines in the Management of Cellulitis in Lymphoedema.

Diagnosis

- The symptoms and signs of erysipelas and cellulitis reflect inflammation secondary to bacterial invasion. Differentiating infectious from non-infectious inflammatory responses can be challenging.
- The likelihood of cellulitis can be assessed through the ALT-70 score* (https://www.mdcalc.com/alt-70-score-cellulitis):
    - Asymmetric: Yes, 3 points; No, 0 points.

    - Leukocytosis: ≥ 10.00 x 10^9/L, 1 point; < 10.00 x 10^9/L, 0 points.
    - Tachycardia: ≥ 90 bpm, 1 point; < 90 bpm, 0 points.
    - ≥ 70 years: Yes, 2 points; No, 0 points.
- Scores:
    - 5-7: likely cellulitis.
    - 3-4: consider infectious and non-infectious differential diagnoses.
    - 0-2: unlikely cellulitis, consider non-infectious differential diagnoses.

* Please note the MDCalc statement “Use in adult patients presenting to the ED with a red leg and clinical concern for cellulitis. Do not use if: visible abscess/fluctuance, penetrating trauma, burn, diabetic ulcer, hardware/device, post-operative patient, or recent (within 48 hrs) IV antibiotic use.”

Differential diagnosis

- The pain, erythema, warmth, tenderness, and swelling of inflammation can be secondary to non-infectious disease.
- Reflected in the ALT-70 scoring:
    - Patients with bilateral/symmetric stigmata; and
    - Patients without systemic responses

  Require consideration of non-infectious disease.
- Non-microbial mimickers include vascular and inflammatory aetiologies. Common causes of pseudocellulitis include venous stasis dermatitis, venous stasis ulcers, gout/pseudogout, congestive heart failure, non-specific oedema, deep venous thrombosis, and acute lipodermatosclerosis.

Investigation

Symptoms and signs provide the criteria for the diagnosis of erysipelas and cellulitis. The investigations outlined herein provide guidance for treatment, rather than diagnostic criteria.

Microbiology

- ± Blood cultures:
    - Bacteraemia is relatively uncommon in erysipelas and cellulitis. However, culture and resistance/susceptibility profiles enable de-escalation and optimisation of antimicrobial chemotherapy. Blood cultures are recommended with:
        - Episode(s) of fever; or
        - If the differential diagnosis includes bloodstream infection, sepsis, or septic shock; or
        - If for initiation of treatment with intravenous antibiotics.
- MRSA screen:
    - *Staphylococcus aureus* can cause erysipelas and cellulitis. If initial empiric therapy is deemed ineffective, broadening the cover to include MRSA can be one therapeutic option. Therefore, MRSA screen is recommended.
- ± Pus swab:
    - For example, if purulent discharge.

Blood sciences

- Full blood count (FBC), C-reactive protein (CRP), ± lactate, urea and electrolytes (U&Es), and liver function tests (LFTs):
    - Signs of erysipelas and cellulitis can deepen initially, with infectious stigmata persisting for weeks. Inflammatory markers (FBC and CRP)

provide objective markers for gauging efficacy of antibiotics and are recommended 24-48 hourly.

Treatment

Intravenous versus per oral antibiotics; community versus hospital

- Criteria for intravenous:
    - (1) Proximity of erysipelas or cellulitis to medical device (e.g. prosthetic joint).
    - (2) Progression of symptoms and signs after 48 hours of per oral antibiotics.
    - (3) Suboptimal vasculature - e.g. chronic venous insufficiency, diabetes mellitus, peripheral vascular disease - impeding delivery of antibiotics.
    - (4) Intolerant of per oral antibiotics.
    - (5) Sepsis.
    - (6) Septic shock.
- Classification for intravenous versus per oral antibiotics, and community versus hospital health care:
    - Class I:
        - No criteria for intravenous.
        - Per oral antibiotics in the community.
    - Class II:
        - Criteria (1), (2), (3), or (4) for intravenous.
        - Consider intravenous therapy via outpatient parenteral antimicrobial therapy (OPAT) in the community, or via the same day emergency care (SDEC)/short term antibiotic therapy (STAT) team in ambulatory care, or in hospital.
    - Class III:
        - Criteria (5) for intravenous.
        - Intravenous therapy in hospital ± in the intensive care unit (ICU).
    - Class IV:
        - Criteria (6) for intravenous.
        - Intravenous therapy in the ICU.

Empiric antibiotics

- Review the past microbiology results, with specific reference to previous soft tissue samples:
    - Culture positive for *Streptococcus* groups A/B/C/G, MSSA, and MRSA:
        - Noting susceptibility or resistance to first-fifth line options for erysipelas and cellulitis.
- NB Re susceptibilities:
    - *Streptococcus* groups A/B/C/G, MSSA, and MRSA that are tetracycline S are also doxycycline S.
    - *Streptococcus* groups A/B/C/G, MSSA, and MRSA that are erythromycin S are also clarithromycin S.
    - Susceptibility of *Streptococcus* groups A/B/C/G, MSSA, and MRSA to clindamycin is, in general, inferred from macrolide (e.g. erythromycin) S.
    - *Streptococcus* groups A/B/C/G that are penicillin S are also amoxicillin S.

- *Streptococcus* groups A/C/G that are penicillin S are also flucloxacillin S.

Empiric, per oral antibiotics

- First line: flucloxacillin 1 g 6 hourly.
- Second line: doxycycline 100 mg 12 hourly.
- Third line: clarithromycin 500 mg 12 hourly.
- Fourth line: clindamycin 300 mg 6 hourly.
- Fifth line: linezolid 600 mg 12 hourly.

Empiric, outpatient parenteral antimicrobial therapy (OPAT)

- First line: ceftriaxone 2 g intravenously 24 hourly.
- Second line: teicoplanin, dosage as per hospital guidelines, target pre dose level 15-30 mg/l.
- Third line: daptomycin 4-6 mg/kg intravenously 24 hourly.

Empiric, same day emergency care (SDEC)/short term antibiotic therapy (STAT)

- First line: ceftriaxone 2 g intravenously for the first 24 hours; ceftriaxone 2 g intramuscularly 24 hourly thereafter.
- Second line: linezolid 600 mg intravenously for the first 12 hours; linezolid 600 mg per oral 12 hourly thereafter.
- Third line: teicoplanin, dosage as per hospital guidelines, target pre dose level 15-30 mg/l.

- Ceftriaxone, linezolid, or teicoplanin for ≤ 3 days.
- If ambulatory care deems the response satisfactory, transition from intravenous to per oral antibiotics.
- If unsatisfactory, intravenous therapy via OPAT or in hospital.

Empiric, intravenous antibiotics

- First line: flucloxacillin 2 g 6 hourly.
- Second line: teicoplanin, dosage as per hospital guidelines, target pre dose level 15-30 mg/l.
- Third line: clindamycin 600 mg 6 hourly.
- Fourth line: linezolid 600 mg 12 hourly (NB or per oral [absorption 100%]).
- Fifth line: daptomycin 4-6 mg/kg 24 hourly.

Directed, intravenous antibiotics (with susceptibilities)

- *Streptococcus* groups A/B/C/G, according to susceptibilities:
  - First line: benzylpenicillin 1.2 g 6 hourly.
  - Second line: teicoplanin, dosage as per hospital guidelines, target pre dose level 15-30 mg/l.
  - Third line: clindamycin 600 mg 6 hourly.
- Methicillin susceptible *Staphylococcus aureus*, according to susceptibilities:
  - First line: flucloxacillin 2 g 6 hourly.
  - Second line: teicoplanin, dosage as per hospital guidelines, target pre dose level 15-30 mg/l.
  - Third line: clindamycin 600 mg 6 hourly.
- Methicillin resistant *Staphylococcus aureus*, according to susceptibilities:

  - First line: teicoplanin, dosage as per hospital guidelines, target pre dose level 15-30 mg/l.
  - Second line: clindamycin 600 mg 6 hourly.
  - Third line: linezolid 600 mg 12 hourly (NB or per oral [absorption 100%]).

Intravenous to per oral step down

- After 48 hours of intravenous antibiotics, if the patient is afebrile, observations stable, and inflammatory markers downward trending, collaborate with the senior(s) regarding per oral step down.

Directed, per oral antibiotics (with susceptibilities)

- *Streptococcus* groups A/B/C/G, according to susceptibilities:
  - First line: amoxicillin 500 mg 8 hourly.
  - Second line: doxycycline 100 mg 12 hourly.
  - Third line: clarithromycin 500 mg 12 hourly.
- Methicillin susceptible *Staphylococcus aureus*, according to susceptibilities:
  - First line: flucloxacillin 1 g 6 hourly.
  - Second line: doxycycline 100 mg 12 hourly.
  - Third line: clarithromycin 500 mg 12 hourly.
- Methicillin resistant *Staphylococcus aureus*, according to susceptibilities:
  - First line: doxycycline 100 mg 12 hourly.
  - Second line: clarithromycin 500 mg 12 hourly.
  - Third line: clindamycin 300 mg 6 hourly.

Duration of antibiotics

- In general, 5-7 days.
- Consider a prolonged course of 10-14 days if:
  - Proximity of erysipelas or cellulitis to medical device (e.g. prosthetic joint).
  - Suboptimal vasculature – e.g. peripheral vascular disease – impeding delivery of antibiotics.
  - CRP > 100 on days 5-7.
  - Bacteraemia with *Streptococcus* group A.
  - Bacteraemia with *Staphylococcus aureus*.
- Consider a prolonged course of 14 days if:
  - Lymphoedema associated cellulitis.

NB Resolution of erysipelas and cellulitis

- Signs of erysipelas and cellulitis can deepen initially, with infectious stigmata persisting for weeks.
- The deepening and persistence may reflect: lysis of pathogens → causing release of bacterial macromolecules → driving local inflammation.
- Temperature, obs., FBC, and CRP can be utilised to gauge the efficacy of antibiotics.
- Even if the signs of erysipelas and cellulitis deepen initially, or persist:
  - If the temperature settles; if the observations stabilise; if the inflammatory markers ↓

  Then, these objective parameters can be indicative of efficacious antibiotics for diagnoses of erysipelas and cellulitis infectious disease.

Management

Symptoms and signs of erysipelas/cellulitis; ALT-70 score (https://www.mdcalc.com/alt-70-score-cellulitis) ≥ 3

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Investigation
- Microbiology: ± blood cultures, MRSA screen, ± pus swab
- Blood sciences: FBC, CRP, ± lactate, U&Es, and LFTs

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Treatment, criteria for intravenous antibiotics:
- (1) Proximity of erysipelas or cellulitis to medical device (e.g. prosthetic joint)
- (2) Progression of symptoms and signs after 48 hours of per oral antibiotics
- (3) Suboptimal vasculature – e.g. peripheral vascular disease – impeding delivery of antibiotics
- (4) Intolerant of per oral antibiotics
- (5) Sepsis
- (6) Septic shock

No criteria for intravenous	Criteria (1), (2), (3), or (4)	Criteria (5)	Criteria (6)
↓	↓	↓	↓
Class I • Per oral antibiotics in the community	Class II • Intravenous therapy via OPAT in the community, or via the SDEC/STAT team in ambulatory care, or in hospital	Class III • Intravenous therapy in hospital ± in the ICU	Class IV • Intravenous therapy in the ICU

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Empiric antibiotics (please note, pages 3-4)

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Directed antibiotics with culture and susceptibilities (please note, pages 4-5)

Appendix

- Manifold classifications of infection exist, including skin infectious disease:
    - Eron devised one classification scheme in 2000.
    - CREST another in 2005:
        - "Class I patients have no signs of systemic toxicity, have no uncontrolled co-morbidities and can usually be managed with oral antimicrobials on an outpatient basis."
        - "Class II patients are either systemically ill or systemically well but with a co-morbidity such as peripheral vascular disease, chronic venous insufficiency or morbid obesity which may complicate or delay resolution of their infection."
        - "Class III patients may have a significant systemic upset such as acute confusion, tachycardia, tachypnoea, hypotension or may have unstable co-morbidities that may interfere with a response to therapy or have a limb threatening infection due to vascular compromise."
        - "Class IV patients have sepsis syndrome or severe life threatening infection such as necrotizing fasciitis."
- The intravenous versus per oral antibiotics; community versus hospital section is founded on the Eron and CREST schemes, and expanded upon to reflect the incorporation of modern practices - e.g. OPAT and SDEC/STAT - into the management of erysipelas and cellulitis.

References

Bennett, J. E., Dolin, R., and Blaser, M. J. 2015. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, 8th Edition. Elsevier.
CREST. 2005. Guidelines on the management of cellulitis in adults. Available at: Cellulitis-guidelines-CREST-05.pdf (legsmatter.org).
National Institute for Health and Care Excellence (NICE). 2019. Cellulitis and erysipelas: antimicrobial prescribing. Available at: Overview | Cellulitis and erysipelas: antimicrobial prescribing | Guidance | NICE.
Spelman, D. and Baddour, L. M. 2022. Acute cellulitis and erysipelas in adults: Treatment. Available at: Acute cellulitis and erysipelas in adults: Treatment - UpToDate.
Spelman, D. and Baddour, L. M. 2022. Cellulitis and skin abscess: Epidemiology, microbiology, clinical manifestations and diagnosis. Available at: Cellulitis and skin abscess: Epidemiology, microbiology, clinical manifestations, and diagnosis - UpToDate.
Sullivan, T. and de Barra, E. 2018. Diagnosis and management of cellulitis. Clinical Medicine.
Weng, Q. Y., Raff, A. B., and Cohen, J. M. 2017. Costs and Consequences Associated With Misdiagnosed Lower Extremity Cellulitis. The Journal of the American Medical Association Dermatology.

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