Soft Tissue Infection associated with Water Exposure in Adults - Microbiology Full Clinical Guideline

Reference number: CG-ANTI/2019/067

Introduction

- If skin colonisation with beta-haemolytic streptococci or *Staphylococcus aureus* coincides with skin breach, these bacteria can invade the soft tissues.
- If skin breach is concurrent with exposure to water, the microorganisms resident within fresh, brackish, or seawater can also be inoculated and cause infection.
- Water associated bacterial pathogens include the life threatening, e.g. *Vibrio vulnificus*.
- *Aeromonas* species, *Chromobacterium violaceum*, *Edwardsiella tarda*, and *Shewanella* species are other bacterial species associated with exposure to water.
- Whilst exposure to water necessitates cogitation regarding exotic infectious agents; equally, the more commonly encountered pathogens - beta-haemolytic streptococci and *Staphylococcus aureus* - continue to require consideration in the microbial differential diagnosis.
- Injury to the skin can arise before water contact:
    - 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.
- Injuries to the skin can also be sustained within the water:
    - Trauma: e.g. animal bites, lacerations, punctures from fish hooks/spines.
- Injuries associated with freshwater have a higher risk of soft tissue infection than brackish water. Brackish water, in turn, has a higher risk of soft tissue infection than injuries associated with seawater.

Differential diagnosis: cellulitis

- In soft tissue infection associated with fresh, brackish, or seawater exposure, exotic and/or common bacterial pathogens can invade the dermis and subcutis.
- The invasion and subsequent inflammation can manifest in symptoms and signs, including skin erythema, warmth, tenderness, and swelling.

Differential diagnosis: necrotising soft tissue infection

- The exotic and/or common bacterial pathogens can also cause necrosis of the skin (necrotising cellulitis), fascia (necrotising fasciitis), and/or muscle (necrotising myositis).
- The invasion and subsequent infective-inflammatory mediated occlusion of the vasculature can manifest, again, in skin erythema, warmth, tenderness, and swelling. Crescendo pain (severe, rapid, and requiring narcotic analgesia), dusky-purplish skin, skin bullae (haemorrhagic bullae), and crepitus can be distinguishing features of necrotising soft tissue infection. The life threatening nature of this infectious disease can also manifest in diagnostic criteria for sepsis and septic shock, e.g. hypotension.

- If symptoms, signs, sepsis, and/or septic shock raise the differential diagnosis of necrotising soft tissue infection, immediately collaborate with the relevant surgical registrar/consultant on call.
    - Ophthalmology, maxillofacial, and/or otorhinolaryngology opinions can be required for the head and neck;
    - General surgery and/or obstetrics/gynaecology for the female torso;
    - General surgery and/or urology for the male torso;
    - Orthopaedics for the limbs.
- If surgery suspects necrotising soft tissue infection, surgical intervention is the overriding priority; superseding other management strands, e.g. completion of resuscitation.
- Necrotising soft tissue infection remains a surgically diagnosed infectious disease, and time is tissue for this life threatening infectious disease:
    - Specifically, National Confidential Enquiry into Patient Outcome and Death (NCEPOD) Classification of Intervention:
        - Code: 1.
        - Category: immediate.
        - Description: immediate (A) lifesaving or (B) limb or organ-saving intervention. Resuscitation simultaneous with surgical treatment.
        - Target time to theatre: within 30 minutes.
        - Expected location: next available operating theatre – "break-in" to existing lists if required.

Cellulitis associated with water exposure: investigation

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

Microbiology

- ± Blood cultures:
    - Bacteraemia is relatively uncommon in 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 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 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.

Cellulitis associated with water exposure: treatment

Intravenous versus per oral antibiotics

- Criteria for intravenous:
    - (1) Proximity of 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.

Empiric, per oral antibiotics

- First line: levofloxacin 500 mg 12 hourly.
- Second line: doxycycline 100 mg 12 hourly.
- Third line: co-trimoxazole 960 mg 12 hourly.

Empiric, intravenous antibiotics

- First line:
    - Piperacillin tazobactam 4.5 g 6 hourly **and**:
        - Levofloxacin 500 mg 12 hourly; **or**
        - Doxycycline 100 mg (NB per oral) 12 hourly.
- Second line, if non-immediate without systemic involvement penicillin allergy:
    - Ceftazidime 2 g 8 hourly **and**:
        - Levofloxacin 500 mg 12 hourly; **or**
        - Doxycycline 100 mg (NB per oral) 12 hourly.
- Third line, if immediate rapidly evolving or non-immediate with systemic involvement penicillin allergy:
    - Levofloxacin 500 mg 12 hourly **and**:
        - Doxycycline 100 mg (NB per oral) 12 hourly; **or**
        - Co-trimoxazole 960 mg 12 hourly.

Directed, intravenous antibiotics (with susceptibilities)

- *Aeromonas* species, *Chromobacterium violaceum*, *Edwardsiella tarda*, *Shewanella* species, and *Vibrio vulnificus*:
    - Collaborate with the microbiology consultant.
- *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)

- *Aeromonas* species, *Chromobacterium violaceum*, *Edwardsiella tarda*, *Shewanella* species, and *Vibrio vulnificus*:
  - Collaborate with the microbiology consultant.
- *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

- 10-14 days.

NB Resolution of cellulitis

- Signs of 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 efficacy of antibiotics.
- Even if the signs of 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 the diagnosis of cellulitis.

Necrotising soft tissue infection associated with water exposure; pre-operative management

Investigation

- Blood sciences:
  - FBC, CRP, lactate, U&Es, and LFTs may reveal markers of infection, sepsis, and organ dysfunction, and are recommended.
  - Aspartate aminotransferase or creatine kinase rises are suggestive of necrotising soft tissue infection, and are also recommended.
- Microbiology:
  - Blood cultures x 2-3 may reveal single or multiple pathogens, and are recommended.

    - Methicillin resistant *Staphylococcus aureus* (MRSA) screen is also recommended.
- Radiology:
    - Imaging is NOT recommended:
        - Diagnoses of necrotising soft tissue infection are established via surgical exploration in theatre.
        - Time is tissue for this life threatening infectious disease.

Treatment

- Empiric, intravenous antibiotics within 1 hour:
    - First line:
        - Piperacillin tazobactam 4.5 g 6 hourly **and**:
            - Levofloxacin 500 mg 12 hourly; **or**
            - Doxycycline 100 mg (NB per oral) 12 hourly.
    - Second line, if non-immediate without systemic involvement penicillin allergy:
        - Ceftazidime 2 g 8 hourly **and** metronidazole 500 mg 8 hourly **and**:
            - Levofloxacin 500 mg 12 hourly; **or**
            - Doxycycline 100 mg (NB per oral) 12 hourly.
    - Third line, if immediate rapidly evolving or non-immediate with systemic involvement penicillin allergy:
        - Levofloxacin 500 mg 12 hourly **and** metronidazole 500 mg 8 hourly **and**:
            - Doxycycline 100 mg (NB per oral) 12 hourly; **or**
            - Co-trimoxazole 960 mg 12 hourly.
- NB If clinical concerns re the risk of MRSA, add teicoplanin, dose as per hospital guidelines, target pre dose level 15-30 mg/l.

Necrotising soft tissue infection associated with water exposure; intra-operative management

Investigation

- Microbiology:
    - Surgical samples may reveal single or multiple pathogens. Fluid (≥ 1 ml), pus (≥ 1 ml), and/or tissue (~ 0.5 to 1 cm^3) specimens in universal containers for microscopy (white cell count and differential), culture, and susceptibilities (MC&S) are recommended.
    - Please notify the laboratory during the day (Queen's Hospital Burton, extension 4045; Royal Derby Hospital, extension 88218, option 2) or the microbiology biomedical scientist on call (via switchboard) to enable prompt processing of the surgical samples.

Treatment

- Surgical intervention:
    - In general:
        - Exploration ± debridement of necrotic soft tissues to macroscopically healthy, viable tissue ± amputation.
    - Specifically:
        - Reflecting possible ophthalmology/maxillofacial/ otorhinolaryngology/general surgery/obstetrics and gynaecology/urology/orthopaedic involvement:

- Further specific intervention will vary from specialty to specialty:
    - For example, general surgery may intervene - via laparoscopy - with diversion stoma formation.

Necrotising soft tissue infection associated with water exposure; post-operative management

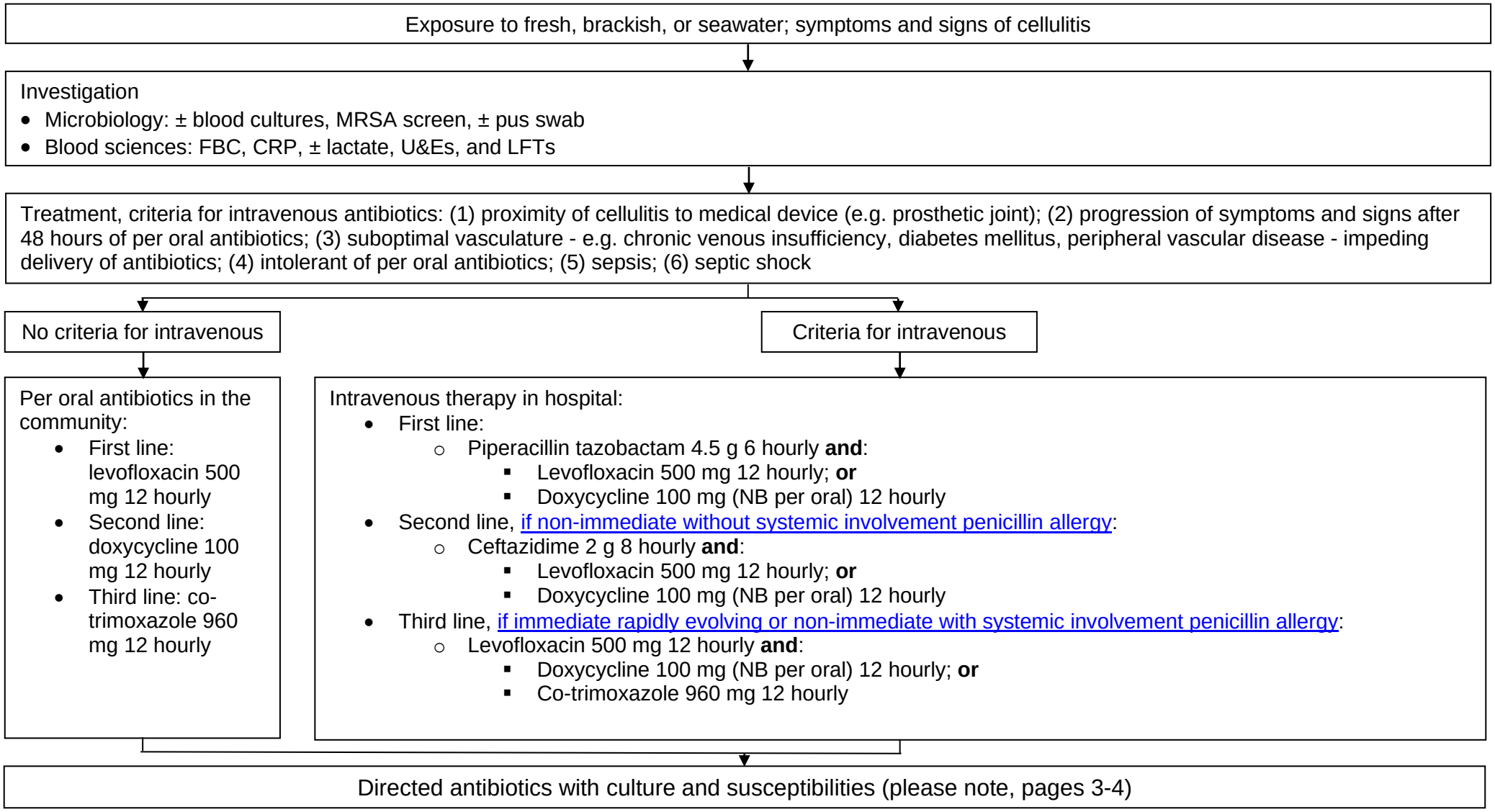
Investigation

- ± Repeat microbiology:
    - Surgical sites can become colonised with human and environmental flora, especially with the administration of antibiotics.
    - Repeat sampling of the debrided surgical site is only recommended:
        - If returned to theatre; and
        - If there is surgical concern re ongoing necrotising soft tissue infection.

Treatment

- Intensive Care Unit (ICU):
    - Post-operatively, to be transferred from theatre to the ICU, with the anaesthetic consultant in theatres to liaise with the intensivist team re transfer of care.
- Surgical interventions:
    - Post-operatively, bacteria may remain within the macroscopically healthy, viable tissue. Therefore:
        - If clinical concerns emerge immediately:
            - Collaborate with the relevant surgical registrar/consultant on call regarding ± return to theatre.
        - If no clinical concerns emerge immediately:
            - Return to theatre ≤ 24 hours after the first/latest surgical intervention for re-inspection.
            - Return to theatre 24-48 hourly thereafter, until the surgical team are satisfied that no necrotic soft tissue remains.
    - With the nature of this infectious disease necessitating, in general, extensive debridement, early consultation with both plastic surgery (regarding reconstruction) and tissue viability are recommended.
- Antibiotics:
    - Empiric, intravenous antibiotics as per pre-operative management.
    - Directed, intravenous and/or per oral antibiotics in collaboration with microbiology.
    - Duration of antibiotics:
        - In general, 10-14 days from the last return to theatre.
        - NB1 Invasive group A streptococcal disease, ≥ 10 days from the last culture of *Streptococcus* group A/*Streptococcus pyogenes*.
        - NB2 Bacteraemia with *Staphylococcus aureus*, ≥ 14 days from the last blood culture of methicillin susceptible *Staphylococcus aureus* or MRSA.

Cellulitis associated with water exposure: management



Necrotising soft tissue infection associated with water exposure: management

Differential diagnosis

- Exposure to fresh, brackish, or seawater; symptoms (e.g. crescendo pain), signs (e.g. haemorrhagic bullae, crepitus), sepsis, or septic shock raising the differential diagnosis of necrotising soft tissue infection

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Diagnosis

- Immediate collaboration with the relevant surgical registrar/consultant on call
- If surgery suspects necrotising soft tissue infection, surgical intervention is the overriding priority
- Time is tissue: NCEPOD code 1 (immediate lifesaving/limb or organ-saving intervention within 30 minutes)

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Pre-operative investigation and treatment

- FBC, CRP, lactate, U&E, LFT. Aspartate aminotransferase or creatine kinase
- Blood cultures x 2-3. MRSA screen
- Empiric, intravenous antibiotics within 1 hour:
  - First line:
    - Piperacillin tazobactam 4.5 g 6 hourly **and**:
      - Levofloxacin 500 mg 12 hourly **or** doxycycline 100 mg (NB per oral) 12 hourly
  - Second line, if non-immediate without systemic involvement penicillin allergy:
    - Ceftazidime 2 g 8 hourly **and** metronidazole 500 mg 8 hourly **and**:
      - Levofloxacin 500 mg 12 hourly **or** doxycycline 100 mg (NB per oral) 12 hourly
  - Third line, if immediate rapidly evolving or non-immediate with systemic involvement penicillin allergy:
    - Levofloxacin 500 mg 12 hourly **and** metronidazole 500 mg 8 hourly **and**:
      - Doxycycline 100 mg (NB per oral) 12 hourly **or** co-trimoxazole 960 mg 12 hourly
  - NB If clinical concerns re the risk of MRSA, add teicoplanin, dose as per hospital guidelines, target pre dose level 15-30 mg/l

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Intra-operative and post-operative investigation and treatment

- Surgical exploration ± debridement ± amputation. Return to theatre ≤ 24 hours after the first surgical intervention for re-inspection. Return to theatre 24-48 hourly thereafter, until the surgical team are satisfied that no necrotic soft tissue remains
- Multiple fluid (≥ 1 ml), pus (≥ 1 ml), and/or tissues (~0.5 - 1 cm^3) in universal containers for MC&S
- Post-operative transfer to ICU
- Early consultation with both plastic surgery (regarding reconstruction) and tissue viability

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