Background

Prompt administration of appropriate antibiotics is vital in the management of patients with sepsis. Delayed treatment of patients with severe infection and sepsis is associated with high mortality rates and high healthcare costs. Effective antimicrobial administration within the first hour of documented hypotension is associated with increased mortality and it has been estimated that the mortality rate increases by 7.6% with every hour’s delay in commencing antibiotic therapy in the first six hours after the onset of hypotension.

Objective

This guideline aims to guide the prescription and timely administration of the FIRST DOSE of intravenous (IV) antibiotics for adult patients who have suspected sepsis or where the sepsis pathway has been initiated in the Emergency Department (please refer to RHH Emergency Department Adult Sepsis Pathway FT043345 ED adult sepsis bundle).

Definitions

SYSTEMIC INFLAMMATORY RESPONSE SYNDROME (SIRS)

Patient has SIRS if they have 2 or more of the following criteria:

- Temperature less than 36°C or greater than 38°C
- White cell count less than 4 or greater than 12
- Respiratory rate greater than 24 per minute
- Heart rate greater than 90 beats per minute

SEPSIS
Patient has sepsis if they have suspected or confirmed infection together with SIRS.

**SEVERE SEPSIS**

Patient has severe sepsis if they sepsis together with organ dysfunction.

**SEPTIC SHOCK**

Patient has septic shock if they have sepsis together with either:

- A systolic blood pressure less than 90 mmHg for one hour despite adequate fluid resuscitation
- OR
- The need for inotropes to maintain the systolic blood pressure more than 90 mmHg

**RHH EMERGENCY DEPARTMENT ADULT SEPSIS PATHWAY**

Please refer to the: [RHH ED Adult Sepsis Pathway](#) for further information.

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**Empirical Antibiotic Therapy**

1. **Microbiology specimens**

   In adult patients with sepsis, obtain two sets of blood cultures before administering antibiotics. Please refer to the: [Blood Culture Collection - RHH - Clinical Protocol - E10](#). Obtain other clinical specimens as appropriate but do not delay administration of antibiotics or wait for results of investigations prior to administration.

2. **Empirical antibiotic therapy**

   Please refer to [Appendix 1](#) for guidance relating to appropriate initial empirical antibiotic regimens for different clinical scenarios.

3. **Special considerations for specific antibiotics**

   **Vancomycin**

   A loading dose should be considered in all patients to facilitate rapid attainment of target serum vancomycin concentration. This should be dosed at 25-30 mg/kg of actual bodyweight and infused
EMPIRICAL ANTIBIOTIC THERAPY FOR SEPSIS IN ADULT PATIENTS

at 10mg/minute. The ongoing dose and dosage interval can be calculated according to the renal function with the next dose due at least 12 hours after the initial loading dose. The table below can be used as a guide:

<table>
<thead>
<tr>
<th>Actual body weight</th>
<th>&lt; 60 kg</th>
<th>60-80 kg</th>
<th>80-100 kg</th>
<th>&gt;100 kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loading dose</td>
<td>1 gram</td>
<td>1.5 grams</td>
<td>2 grams</td>
<td>2.5 grams</td>
</tr>
</tbody>
</table>

Monitoring of vancomycin plasma concentrations is not required if therapy is ceased within 48 hours and renal function is stable. If the plan is to extend therapy beyond 48 hours, monitoring is required.

Please refer to the Vancomycin Guideline - RHH - Clinical Practice Guideline ID-1-0005 for further information if required.

Gentamicin

The initial dose should be dosed at 4-7 mg/kg of lean (ideal) bodyweight (dependant on age) and diluted in 100mL of infusion fluid and infused over 30 minutes. After the initial gentamicin dose, the ongoing indication for gentamicin therapy needs to be reviewed. The dosing interval for subsequent dosing is based on the patient’s renal function.

Gentamicin must not be used in patients with:

- Serious hypersensitivity reaction to aminoglycosides (rare)
- Previous vestibular or auditory toxicity to an aminoglycoside

Gentamicin should be avoided, or if there is no appropriate, safer alternative, used for 48 hours or less in patients with:

- Pre-existing significant hearing problems
- Pre-existing vestibular problems including: dizziness, vertigo or tinnitus
- Neuromuscular disorders (including myasthenia gravis and parkinsonism)
- Chronic renal failure or deteriorating renal function
- Chronic liver disease or severe cholestasis (serum bilirubin greater than 90 micromol/L)

Monitoring of aminoglycoside plasma concentrations is not required if therapy is ceased within 48 hours. If the plan is to extend therapy beyond 48 hours, monitoring is required.

Please refer to the Aminoglycoside for Adult Patients - RHH - Clinical Guideline 1-0004 or the current version of the Therapeutic Guidelines: Antibiotic Version for further information if required.
Beta-lactam antibiotics

ALL penicillin and cephalosporin class antibiotics are contraindicated in patients with IgE-mediated penicillin or cephalosporin allergy OR who have had previous severe drug reactions due to these drug classes (e.g. DRESS (drug rash with eosinophilia and systemic symptoms) syndrome or Stevens-Johnson syndrome).

In the presence of renal impairment, the initial dose is usually unchanged but the subsequent dosing intervals will need to be reviewed as modification may be required. Please refer to the current version of the Therapeutic Guidelines: Antibiotic Version for further information if required.

Follow-up

This guideline refers to the initial empirical IV antibiotics for adult patients who have suspected sepsis or where the sepsis pathway has been initiated in the Emergency Department (please refer to RHH Emergency Department Adult Sepsis Pathway).

The empirical antibiotic regimes are intended for the initial 48-72 hours only and after that time, the initial empirical therapy needs to be reviewed in conjunction with the clinical presentation and the results of the microbiological results:

- If a non-infective diagnosis is made, therapy should be ceased.

- If no proven causative organism has been identified, re-evaluate the clinical and microbiological justification for continuing therapy. If ongoing therapy is indicated, consider de-escalation (e.g. change parenteral therapy to oral therapy for a defined duration).

- If a causative organism has been identified, antimicrobial therapy should be targeted to the particular organism and clinical indication using the most effective, least toxic and narrowest spectrum drug available. The duration of therapy should be kept as short as possible. 7 days of therapy should not be exceeded without a clear indication for a longer duration e.g. endocarditis, osteomyelitis.
EMPIRICAL ANTIBIOTIC THERAPY FOR SEPSIS IN ADULT PATIENTS

References


Acknowledgements and Stakeholders

- Department of Infectious Diseases and Microbiology
- Department of Pharmacy
- Department of Emergency Medicine
- Department of Critical Care Medicine

Related Documents

RHH Emergency Department Adult Sepsis Pathway

Key Words - Intranet Search Function

1. Sepsis
2. Sepsis pathway
3. Empirical antibiotics

Appendix 1. A3 Summary Chart: Guideline for Empirical Antibiotic Therapy in Adult Patients with Sepsis
**Likely source of sepsis**

<table>
<thead>
<tr>
<th><strong>Sepsis, unknown source (immunocompetent patient)</strong></th>
<th><strong>Empirical antibiotic regimen</strong></th>
<th><strong>Non-life-threatening penicillin allergy or reaction</strong></th>
<th><strong>Severe penicillin or cephalosporin reaction</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>1. intravenous cannulae)</td>
<td>Flucloxacillin 2g IV 6-hourly AND gentamicin**4-7mg/kg IV for 1 dose</td>
<td>Cefazolin 2g IV 8-hourly AND gentamicin**4-7mg/kg IV for 1 dose</td>
<td>Vancomycin*1 to 2.5g IV loading dose AND gentamicin**4-7mg/kg IV for 1 dose</td>
</tr>
<tr>
<td>2. Sepsis and meningococcal infection suspected</td>
<td>Flucloxacillin AND gentamicin** AND clindamycin 600mg IV 8-hourly</td>
<td>Cefazolin AND gentamicin** AND clindamycin 600mg IV 8-hourly</td>
<td>Vancomycin* AND gentamicin** AND clindamycin 600mg IV 8-hourly</td>
</tr>
<tr>
<td>3. Sepsis and toxin mediated shock suspected</td>
<td>Flucloxacillin AND gentamicin** AND clindamycin 600mg IV 8-hourly</td>
<td>Cefazolin AND gentamicin** AND clindamycin 600mg IV 8-hourly</td>
<td>Vancomycin* AND gentamicin** AND clindamycin 600mg IV 8-hourly</td>
</tr>
</tbody>
</table>

**Febrile neutropenia without systemic compromise**
- Consider adding vancomycin if there is concern regarding vascular access device infection or MRSA infection

**Febrile neutropenia with systemic compromise**
- Refer: Empirical antimicrobial therapy in adult haematology and oncology patients presenting with febrile neutropenia

**Severe community acquired pneumonia (CORB ≥2)**
- Refer: RHH Adult CAP guideline

**Sepsis and toxin mediated shock suspected**
- Consider dexamethasone starting before or with the first antibiotic dose. Consider adding vancomycin if there is concern regarding 5. pneumoniae meningitis

**Meningitis**
- Consider dexamethasone starting before or with the first antibiotic dose. Consider adding vancomycin if there is concern regarding 5. pneumoniae meningitis

**Urinary**
- Flucloxacillin 2g IV 6-hourly AND gentamicin**4-7mg/kg IV for 1 dose | Ceftriaxone 1g IV daily AND azithromycin 500mg IV daily | Gentamicin**4-7mg/kg IV for 1 dose AND metronidazole 500mg IV 12-hourly |

**Biliary, gastrointestinal tract or intra-abdominal source**
- Amoxicillin 1g IV 6-hourly AND gentamicin**4-7mg/kg IV for 1 dose | Ceftriaxone 1g IV daily AND azithromycin 500mg IV daily | Gentamicin**4-7mg/kg IV for 1 dose AND metronidazole 500mg IV 12-hourly |

**Meningitis**
- Ceftriaxone 2g IV 12-hourly AND benzylpenicillin 2.4g IV 4-hourly | Ceftriaxone 2g IV 12-hourly | Vancomycin*1 to 2.5g IV loading dose AND moxifloxacin 400mg IV daily |

**Skin or bone/joint**
- Flucloxacillin 2g IV 6-hourly | Cephalazolin 1g IV daily AND azithromycin 500mg IV daily | Clindamycin 600mg IV 8-hourly |

**Diabetic foot**
- Piperacillin-tazobactam 4.5g IV 8-hourly | Cephalazolin 1g IV daily AND azithromycin 500mg IV daily | Clindamycin 600mg IV 8-hourly AND gentamicin**4-7mg/kg IV for 1 dose |

**Necrotising skin and soft tissue**
- Meropenem 1g IV 8-hourly AND clindamycin 600mg IV 8-hourly | Cefepime 2g IV 8-hourly AND azithromycin 500mg IV daily | Clindamycin 600mg IV 8-hourly AND gentamicin**4-7mg/kg IV for 1 dose |

**Female genital tract**
- Ceftriaxone 1g IV daily AND azithromycin 500mg IV daily AND metronidazole 500mg IV 12-hourly | Ceftriaxone 1g IV daily AND azithromycin 500mg IV daily AND metronidazole 500mg IV 12-hourly | Ceftriaxone 1g IV daily AND azithromycin 500mg IV daily AND metronidazole 500mg IV 12-hourly |

**Vascular access device related (including peripheral intravenous cannulae)**
- Flucloxacillin 2g IV 6-hourly AND gentamicin**4-7mg/kg IV for 1 dose | Ceftriaxone 2g IV 8-hourly AND gentamicin**4-7mg/kg IV for 1 dose | Vancomycin*1 to 2.5g IV loading dose AND gentamicin**4-7mg/kg IV for 1 dose |

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