

empirical therapy - febrile neutropenia

empirical therapy - adults

empirical therapy - children

bacteraemia

- In febrile neutropenic patients, with neutrophils less than $0.5 \times 10^9/L$, or less than $1 \times 10^9/L$ with a predicted decline to less than $0.5 \times 10^9/L$, and fever $>38^\circ C$, urgent empirical IV therapy with broad-spectrum antimicrobials is a universally accepted principle, but debate continues on the optimal regimen.

- Bacteraemia due to *Pseudomonas aeruginosa* occurs relatively infrequently but, because morbidity and mortality are high, empirical regimens usually cover this microorganism.

- The choice of antimicrobials will also depend on local susceptibility patterns. Therapy should be reviewed when a causative organism is identified and susceptibilities are known. Suggested regimens are:

1. ceftazidime 2 g (child: 50 mg/kg up to 2 g) IV, 8-hourly
OR
2. piperacillin+tazobactam 4+0.5 g (child: 100+12.5 mg/kg up to 4+0.5 g) IV, 8-hourly
OR
3. gentamicin 4 to 6 mg/kg (child <10 years: 7.5 mg/kg; >10 years: 6 mg/kg) IV, daily
PLUS
ticarcillin+clavulanate 3+0.1 g (child: 50+1.7 mg/kg up to 3+0.1 g) IV, 6-hourly
OR
4. cefepime 2 g (child: 50 mg/kg up to 2 g) IV, 12-hourly.

- Due to the impact of intravascular device related sepsis, bacteraemias due to Gram-positive organisms now predominate. However, vancomycin should not be used presumptively in febrile neutropenic patients unless the patient is in shock, known to be colonised with MRSA, or has clinical evidence of a catheter-related infection in a unit with a high incidence of MRSA infection.

- although it is common practice to add vancomycin to the initial regimen after 48 hours if fever persists, no significant benefit has been demonstrated in controlled trials. Vancomycin is indicated if a Gram-positive organism resistant to other drugs is isolated from blood culture or if the patient has progression of a clinical infection:

vancomycin 25 mg/kg up to 1 g (child <12 years: 30 mg/kg up to 1 g) IV, 12-hourly (monitor levels)

- If fevers persist in high-risk patients beyond 96 hours of antibacterial therapy, consider adding empirically an antifungal drug such as fluconazole, amphotericin B or voriconazole. This is particularly pertinent for patients with radiological evidence of progressive pulmonary infiltrates where an antifungal drug that is active against *Aspergillus* (eg voriconazole or amphotericin B) should be chosen.

- for empirical therapy of severe sepsis with no obvious source of infection in an immunocompetent adult, use:

flucloxacillin 2 g IV, 4- to 6-hourly

PLUS

ceftriaxone 1g IV daily

- For patients hypersensitive to penicillin (excluding immediate hypersensitivity), substitute for flucloxacillin:

cephalothin 2 g IV, 6-hourly

OR

cephazolin 2 g IV, 8-hourly.

For patients with immediate penicillin hypersensitivity, substitute for flucloxacillin: vancomycin 25 mg/kg up to 1 g IV, 12-hourly (monitor blood levels)

- If meningococcal infection is suspected, add benzylpenicillin

- If there is a high prevalence of community-associated MRSA (CA-MRSA) or hospital-acquired MRSA, a regimen of vancomycin plus ceftriaxone should be considered for empirical therapy.

- Although CA-MRSA is an increasing cause of skin and soft tissue infections, bacteraemia is still uncommon. Vancomycin is therefore rarely needed in empirical therapy of community-associated infection, but should be used in patients who are known MRSA carriers.

Meningitis not excluded

- For empirical therapy of severe sepsis with no obvious source of infection in children under 6 months of age in whom meningitis has not been excluded, use:

amoxy/ampicillin 50 mg/kg IV, 6-hourly

PLUS

cefotaxime 50 mg/kg IV, 6-hourly

PLUS (if pneumococcal meningitis is likely)

vancomycin 15 mg/kg IV, 6-hourly (monitor blood levels)

- For children aged 6 months and older, use:

flucloxacillin 50 mg/kg up to 2 g IV, 6-hourly

PLUS EITHER

cefotaxime 50 mg/kg up to 2 g IV, 6-hourly

OR

ceftriaxone 100 mg/kg up to 4 g IV, daily

or ceftriaxone 50 mg/kg up to 2 g IV, 12-hourly

PLUS (if pneumococcal meningitis is likely)

vancomycin 15 mg/kg up to 500 mg IV, 6-hourly (monitor blood levels)

Meningitis excluded

- For empirical therapy of severe sepsis with no obvious source of infection in children under 4 months of age in whom meningitis has been excluded, use:

amoxy/ampicillin 50 mg/kg IV, 6-hourly

PLUS

gentamicin 7.5 mg/kg IV, daily (adjust dose for renal function)

- For children aged 4 months and older, to cover Gram-negative and *Staph aureus* infection, use:

di/flucloxacillin 50 mg/kg up to 2 g IV, 6-hourly

PLUS EITHER

cefotaxime 25 mg/kg up to 1 g IV, 6-hourly

OR

ceftriaxone 25 mg/kg up to 1 g IV, daily.