Canterbury District Health Board
Te Poari Hauora ō Waitaha

Antimicrobial Stewardship Bulletin

CDHB Hospital Antimicrobial Stewardship Committee
Contact: sharon.gardiner@cdhb.health.nz
May 2022 No. 039

PINK BOOK EMPIRIC ANTIMICROBIAL GUIDELINE UPDATE

Sepsis (mate whakatāoke) without apparent source

- **THE PINK BOOK** includes a range of antimicrobial guidelines to be used for sepsis with and without a focus:
  - non-immunosuppressed sepsis without apparent source.
  - immunosuppressed sepsis without apparent source.
  - if there is a focus, see specific guideline e.g. urinary tract infection, meningitis, cholecystitis/cholangitis.
  - after surgery, see presumed septicaemia.
  - after transrectal ultrasound-guided prostate biopsy, see post-TRUS sepsis.
- This bulletin outlines our changes to the first two guidelines, non-immunosuppressed and immunosuppressed sepsis without apparent source. The update was triggered by high local *E. coli* resistance to amoxicillin+clavulanic acid (~26-28%) – keep a look out for our future antimicrobial stewardship bulletin on amoxicillin+clavulanic acid.
- Antimicrobial guidance in the Sepsis in Adults Hospital HealthPathway and in other local resources (e.g. Emergency Department Immunosuppressed Patients pathway) will be updated to align shortly.

NEW PINK BOOK GUIDELINES FOR SEPSIS WITHOUT APPARENT SOURCE

NON-IMMUNOSUPPRESSED

Community-acquired or healthcare-associated
No apparent source

FIRST CHOICE:
CEFTRIAXONE IV 2g every 24 hours

IF HYPOTENSION AND/OR NEW ORGAN DYSFUNCTION:
ADD GENTAMICIN IV 7mg/kg single dose
(CrCl < 20mL/min: PIPERACILLIN+TAZOBACTAM IV 4.5g every 12 hours alone)

IMMUNOSUPPRESSED

No apparent source

FIRST CHOICE:
PIPERACILLIN+TAZOBACTAM IV 4.5g every 6 hours

MILD PENICILLIN ALLERGY:
CEFEPIME* IV 2g every 8 hours

IF HYPOTENSION AND/OR NEW ORGAN DYSFUNCTION:
ADD GENTAMICIN IV 7mg/kg single dose
(CrCl < 20mL/min: consult Infection Management/Microbiology)

VARIATIONS

Apply to both above guidelines

- **MRSA colonised**: ADD vancomycin to the above
- **ESBL colonised**: meropenem IV 1g every 8 hours alone
- **Severe penicillin allergy**: meropenem IV 1g every 8 hours alone
- **Cephalosporin allergy**: consult Infection Management Service

**If intra-abdominal source is possible, add metronidazole to cefepime (not required with piperacillin+tazobactam which has good anaerobic cover). If intra-abdominal source is probable, see cholecystitis/cholangitis.*

COMMENTS AND EXPLANATIONS:

- **Guideline names have been revised** from a focus on neutrophil count (non-neutropenic and neutropenic) to a broader definition of immunosuppression (non-immunosuppressed and immunosuppressed)**.** A drop box has been added to explain what constitutes 'immunosuppression' for this guideline.
- **β-lactam monotherapy is first choice for sepsis without apparent source unless allergic**.
  - non-immunosuppressed: ceftriaxone replaces amoxicillin+clavulanic acid mainly due to higher *E. coli* susceptibility (94% vs 72%; see antibiogram).
  - immunosuppressed: piperacillin+tazobactam is first choice and is now dosed 6-hourly to help ensure concentrations are adequate; cefepime has been added for mild penicillin allergy.
- **A single dose of gentamicin is added to β-lactam therapy in more severe sepsis (hypotension and/or new organ dysfunction).** Reserving gentamicin for the sickest patients better balances the benefits of slightly broader spectrum of cover with the potential harms that may result from its use (vestibular toxicity is rare but is debilitating and usually permanent).
- **Alternative antimicrobial regimens** are provided for those colonised methicillin resistant *S. aureus* (MRSA) or extended spectrum β-lactamase (ESBL) producing gram-negative bacteria (see box).
- **In severe penicillin allergy,** meropenem may be used (risk of cross-reactivity < 1%). In cephalosporin allergy, consultation with the Infection Management Service is advised as the cross-reactivity risk is greater.
- **The interaction between meropenem and valproate** (swift decrease in valproate concentrations by ~70%) is now highlighted under all meropenem entries.
- **Measurement of piperacillin+tazobactam and meropenem trough concentrations** is recommended for those on these agents for over 48 hours, with the Infection Management Service consulted for advice.