Empiric Management of SEPSIS

DEFINITIONS

Sepsis: Life-threatening organ dysfunction caused by aberrant host response to infection. Life-threatening **organ dysfunction** is identified by ≥ 2 points increase in the Sequential [Sepsis-related] Organ Failure Assessment (SOFA) score.

Septic shock: Sepsis accompanied by circulatory failure (requiring vasopressor therapy to maintain MAP ≥ 65 mm Hg) and cellular/metabolic abnormalities (serum lactate > 2 mmol/L despite adequate fluid resuscitation).

Initial management ("sepsis bundle") should be initiated within 1 hour.

MOST COMMON BACTERIAL ORGANISMS

- Dependent on source of infection, setting (community, hospital-associated), patient factors
- ***E. coli, S. aureus, coagulase-negative Staphylococci, Klebsiella sp and S. pneumoniae*** account for ~50% of bloodstream infections in critically ill adults across Canada

Consider invasive fungal (Candida) infection if:

- Severe immunocompromise (HSCT with high Immunodeficiency Scoring Index, neutropenia, immunosuppressive drugs)
- TPN
- Prolonged broad-spectrum antibiotic use
- Recent fungal infection

MICROBIOLOGICAL DIAGNOSTICS

- **BEFORE starting antibiotics**:
  - **2 sets of blood cultures (ideally from peripheral access)**
  - Failure to collect cultures before antibiotics reduces yield by ~35%
  - If symptoms, urine for urinalysis and culture
- Culture other sites according to clinical symptoms/suspected source

To identify patients at high risk of mortality outside of ICU, quick SOFA (qSOFA) score:

Parameter	No	Yes
Altered mental status GCS < 15	0	1
Respiratory rate ≥ 22	0	1
Systolic BP ≤ 100	0	1

TOTAL score	In-hospital mortality
0-1	Not high risk
2-3	HIGH risk

For ICU patients, use SOFA https://www.mdcalc.com/sequential-organ-failure-assessment-sofa-score

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EMPIRIC PHARMACOLOGIC MANAGEMENT[1]

Source unclear - Undifferentiated	Piperacillin-tazobactam 4.5 g IV q8h (after initial bolus dose, extended-infusion over 3-4 hours preferred) *If severe penicillin allergy:* Meropenem 1 g IV q8h
If high risk for invasive fungal infection If known MRSA colonized	Add Caspofungin 70 mg IV on day 1 then 50 mg IV q 24h Add Vancomycin[1] 25 mg/kg IV x 1 then 15 mg/kg IV q12h
Suspected pulmonary source	
Community-acquired	Ceftriaxone 2 g IV q24h **+** azithromycin 500 mg IV q24h *If severe penicillin allergy:* Moxifloxacin 400 mg IV q24h
Hospital-acquired	Piperacillin-tazobactam 4.5 g IV q8h (after initial bolus dose, extended-infusion over 3-4 hours preferred) *If severe penicllin allergy:* Meropenem 1 g IV q8h
Suspected urinary source	Piperacillin-tazobactam 4.5 g IV q8h *If severe penicillin allergy:* Meropenem 1 g IV q8h
If known ESBL colonization/infection within last 6 months	Meropenem 1 g IV q8h
Suspected intra-abdominal infection	Piperacillin-tazobactam 4.5 g IV q8h (after initial bolus, extended-infusion over 3-4 hours preferred) *If severe penicillin allergy:* Ciprofloxacin 400 mg IV q12h + Metronidazole 500 mg IV q8h *If penicillin-allergy and requiring vasopressors:* Meropenem 1g IV q8h
Suspected necrotizing skin and soft tissue infection (with toxic shock syndrome)	Piperacillin-tazobactam 4.5 g IV q8h (extended-infusion over 3-4 hours preferred) + vancomycin[1] 25 mg/kg IV x 1 then 15 mg/kg IV q12h + clindamycin 900 mg IV q8h

[1]Dosing of antibiotics assume normal renal function. Adjustments are required if presence of renal dysfunction. For vancomycin, see Vancomycin Therapeutic Drug Monitoring guideline.

ADDITIONAL CONSIDERATIONS

- **De-escalate antimicrobial therapy as soon as possible after culture results**
- **Source control** (e.g. drain abcess, surgery) as soon as possible.
- Fluid ressuscitation with Ringer's Lactate or other crystalloid solution rather than NS
- If septic shock unresponsive to adequate volume resuscitation and requiring on-going vasopressor therapy after 24h, adjunctive corticosteroids may be indicated (hydrocortisone 50 mg IV q6h)

DATA ON RESISTANCE at MUHC

- *S.aureus:* 3% of clinical isolates are methicillin-resistant (MRSA)
- *E. coli* and *Klebsiella sp:* 8-16% of blood isolates resistant to cephalosporins (ESBL); no *blood* isolates resistant to carbapenems so far.

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