Antimicrobial Treatment of Ventilator-Associated Pneumonia (VAP)

(New Brunswick Provincial Health Authorities Anti-Infective Stewardship Committee, May 2018)

Definition: Pneumonia that develops 48 hours or more after endotracheal intubation.
Probable pathogens: *S. aureus* (MRSA or MSSA), gram-negative bacilli (e.g., *E. coli, K. pneumoniae, P. aeruginosa, A. baumannii*)
Microbiological analyses (always order): Blood cultures x 2 sets + endotracheal suctioning for culture

Risk stratification	Empiric therapy[∞]	Comments
If NO risk factors (indicated below)	First-line piperacillin-tazobactam 4.5 g IV q6h* If **true immediate penicillin allergy**[▲]: meropenem 500 mg IV q6h* If **severe delayed reaction**[‡] to a beta-lactam levoFLOXacin 750 mg IV q24h* **+** tobramycin 7 mg/kg IV q24h*	• Consider adding empiric vancomycin (target trough 15-20 mg/L) in patients with septic shock requiring vasopressors, or with a risk factor for MRSA: o History of MRSA infection or colonization o Injection drug use o Homelessness o Member of First Nations community o Incarcerated person o Recent travel to an MRSA endemic region • If history of infection or colonization with Gram-negative bacilli producing AmpC or ESBL beta-lactamases, empiric use of meropenem is encouraged. • If the patient received an antibiotic in the past 3 months, choose an antibiotic from a different class, regardless of clinical success. • **Second anti-pseudomonal agents** should be from another class, and can include: o tobramycin 7 mg/kg IV q24h* o ciprofloxacin 400 mg IV q8h*
Risk factors for MDR pathogens or poor outcomes ☐ Septic shock requiring vasopressors ☐ Use of IV antibiotics in past 90 days ☐ Immunosuppression ☐ Chronic lung disease (e.g., bronchiectasis, cystic fibrosis) ☐ Acute renal replacement therapy before VAP onset ☐ Hospitalization for at least 5 days before VAP onset ☐ Acute respiratory distress syndrome (ARDS) before VAP onset	First-line piperacillin-tazobactam 4.5 g IV q6h* **+** 2nd anti-pseudomonal agent *(**+/-** vancomycin 25 mg/kg IV x 1 dose, then 15 mg/kg IV q8h*; see comments)* If **true immediate penicillin allergy**[▲] meropenem 500 mg IV q6h* **+** 2nd anti-pseudomonal agent *(**+/-** vancomycin 25 mg/kg IV x 1 dose, then 15 mg/kg IV q8h*; see comments)* If **severe delayed reaction**[‡] to a beta-lactam levoFLOXacin 750 mg IV q24h* **+** tobramycin 7 mg/kg IV q24h* **+** vancomycin 25 mg/kg IV x 1 dose, then 15 mg/kg IV q8h*	
If presence of at least one risk factor (indicated above)		

Duration of therapy

- **Treat for no more than 7 days if good clinical response, regardless of bacterial etiology.**
- Treatment duration could be prolonged for more than 7 days in certain situations (e.g., empyema, extrapulmonary infections, *S. aureus* bacteremia, immunosuppression, etc.)

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Clinical Pearls

- Recent studies have shown that, compared with standard treatment durations of 10 days or more, 7-day treatment durations were associated with fewer relapses caused by multiresistant pathogens WITHOUT affecting mortality rate.
- To avoid prolonged use of broad-spectrum antibiotics, it is essential to de-escalate therapy according to the results of microbiologic analyses.
- The role of antimicrobials in the treatment of ventilator-associated tracheobronchitis[¶] is controversial. Consider initiating antimicrobial therapy if clinical deterioration (e.g. progressive hypoxemia).
- Empiric double coverage of *Pseudomonas aeruginosa* is to maximize the likelihood of having at least one active agent (due to increased risk of resistance with *Pseudomonas*). If *Pseudomonas* is isolated, step-down to monotherapy (according to susceptibility data). ***Use of aminoglycosides (e.g., tobramycin and gentamicin) as monotherapy for the treatment of pneumonia is NOT recommended (even if susceptibility is confirmed).
- DO NOT use DAPTOmycin to treat pneumonia; DAPTOmycin is inactivated by pulmonary surfactant. If MRSA infection, use vancomycin (or linezolid if vancomycin is ineffective or inappropriate).
- Serial procalcitonin levels (if available), in combination with clinical evaluation, may assist in the decision to discontinue antibiotics.

* Dose adjustment required in renal impairment.
∞ If microbial cause of infection known, treat accordingly.
▲ Immediate, IgE mediated allergies include, but are not limited to, anaphylaxis, urticaria, angiœdema, hypotension, bronchospasm, stridor, and pruritic rash.
‡ Severe delayed hypersensitivity reactions to beta-lactams are caused by mechanisms that are not well known and require that subsequent use of beta-lactams be avoided. Severe delayed hypersensitivity reactions can include interstitial nephritis, immune hepatitis, hemolytic anemia, serum sickness, severe cutaneous reactions such as Stevens-Johnson syndrome, toxic epidermal necrolysis, and drug rash with eosinophilia and systemic symptoms (DRESS).
¶ Ventilator-associated tracheobronchitis: fever with no other identifiable cause with: significant purulent secretions, positive endotracheal aspirate culture, and ABSENCE of pneumonia on a chest X-ray.

References:

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2. Pugh R, Grant C, Cooke RP, Dempsey G. Short-course versus prolonged-course antibiotic therapy for hospital-acquired pneumonia in critically ill adults. Cochrane Database Syst Rev 2015; 8:Cd007577
3. Blondel-Hill E. & Fryters S. (2012). Bugs & Drugs. An Antimicrobial/Infectious Diseases Reference. Alberta Health Services.
4. MSH+UHN Antimicrobial Stewardship Program. Hospital Acquired Pneumonia. Accessed online 12-2016.
5. Management of Penicillin and Beta-Lactam Allergy. NB-ASC. 02-2016
6. Adult Antimicrobial Dosing Tool. NB-ASC. 11-2015