

ANTIBIOTIC PROTOCOL FOR ADULT NOSOCOMIAL PNEUMONIA EMPIRIC THERAPY

This pathway is to be used in adult (>18 yo) patients only. An Infectious Diseases consult is recommended when dealing with complicated patients or immunocompromised patients (e.g., hematopoietic stem cell or solid organ transplant). All dosages are based on normal renal and hepatic function.

A. No known Risk Factors for Multidrug-Resistant (MDR; see table below) Pathogens and Early Onset Disease (< 5 d of hospital admission)

Ceftriaxone 1 gram (2 grams if > 80 kg) IV qday **OR**
Levofloxacin^a 750 mg PO/IV qday **OR**
Ampicillin/sulbactam 3 grams IV q6h

B. Known Risk Factors for MDR Pathogens (see table below) or Late Onset Disease (≥ 5 d of hospital admission)

Vancomycin per pharmacy consult 15 mg/kg q12h^{b,c}

PLUS

Cefepime 1 gram IV q6h^d **OR**
Piperacillin/tazobactam 4.5 grams IV q8h, infused over 4 hours

Consider the addition of following agents based on risk factors, clinical presentation, and severity illness

+/- Azithromycin 500mg PO/IV q24h^e
+/- Tobramycin 7 mg/kg IV EIAD^g

Severe beta-lactam allergy:

Vancomycin per pharmacy consult 15 mg/kg q12h^{b,c} **PLUS**
Aztreonam 2 grams IV q8h

Consider the addition of following agents based on risk factors, clinical presentation, and severity illness

+/- Azithromycin 500mg PO/IV q24h^e
+/- Levofloxacin 750mg PO/IV q24h^f
+/- Tobramycin 7 mg/kg IV EIAD^g
+/- Clindamycin 600mg IV q8h^h

^aNot recommended for use during pregnancy.

^bTrough levels for vancomycin should be approximately 15-20 mg/L, a loading dose of vancomycin 25 mg/kg is suggested in severely ill patients

^cLinezolid 600 mg 12h may be used in place of vancomycin

^dCefepime 2g IV q8h if neutropenia

^eIf Legionella is suspected, add azithromycin.

^fIf high risk for pneumococcus, add levofloxacin. DO NOT use both azithromycin and levofloxacin together

^gExtended interval aminoglycoside dosing – Consult the pharmacist for pharmacokinetic evaluation.

^hAdd if aspiration or anaerobic infection is suspected

RISK FACTORS FOR MULTIDRUG-RESISTANT ORGANISMS

- Broad spectrum antimicrobial therapy in preceding 90 d
- Current hospitalization of 5 d or more
- High frequency of antibiotic resistance in the community or the specific hospital unit (antibiogram at www.nebraskamed.com/asp)
- Presence of risk factors for HCAP:
 - Hospitalization for 5 d or more in the preceding 90 d
 - Residence in a nursing home or extended care facility
 - Home infusion therapy (including antibiotics)
 - Chronic dialysis within 30 d
 - Home wound care
 - Family member with multidrug-resistant pathogen
- Immunosuppressive disease and/or therapy

Check pneumococcal and influenza vaccination eligibility and status.
Give vaccinations if indicated.

Hospital, Ventilator and Health Care Associated Pneumonia Pathway

PURPOSE:

To provide a framework for the initial evaluation and management of the immunocompetent, adult patient with bacterial causes of HAP, VAP, or HCAP based on recent literature and guidelines. Delays in the initiation of appropriate antibiotic therapy can increase mortality, and therapy should not be postponed for the purpose of performing diagnostic studies in patients who are clinically unstable.

DEFINITIONS:

Hospital Acquired Pneumonia (HAP) is defined as pneumonia that occurs 48 hours or more after admission, which was not incubating at the time of admission.

Ventilator Acquired Pneumonia (VAP) is defined as pneumonia that arises more than 48–72 hours after endotracheal intubation.

Healthcare Associated Pneumonia (HCAP) includes pneumonia within 48 hours of hospital admission in any patient who was hospitalized in an acute care hospital for five or more days within 90 days of the infection; resided in a nursing home or long-term care facility; received recent intravenous antibiotic therapy, chemotherapy, or wound care within the past 30 days of the current infection; or attended a hospital or hemodialysis clinic.

DIAGNOSIS:

The clinical diagnosis of HAP, VAP and HCAP can be made if the patient has a new radiographic infiltrate PLUS at least two of the following: fever > 38°C, leukocytosis or leucopenia, or purulent secretions. Etiologic diagnosis generally requires a lower respiratory tract culture, but rarely may be made from blood or pleural fluid cultures.

To facilitate etiologic diagnosis, early bronchoalveolar lavage (BAL) sampling, either by mini-BAL technique plus semi-quantitative culture or conventional bronchoscopy with lavage and semi-quantitative culture, should be considered. The probability for a specimen with high yield is highest when the specimen is obtained early (before empiric antimicrobial therapy is started).

MANAGEMENT:

All patients with suspected HAP/VAP/HCAP should have a lower respiratory tract sample and blood sent for culture, and patients with HAP and HCAP should have sputum samples sent whenever possible before the administration of antibiotic therapy. Extrapulmonary infection should be excluded as part of the evaluation

Unless there is low clinical suspicion for lower respiratory tract infection, empiric antibiotics should be initiated.

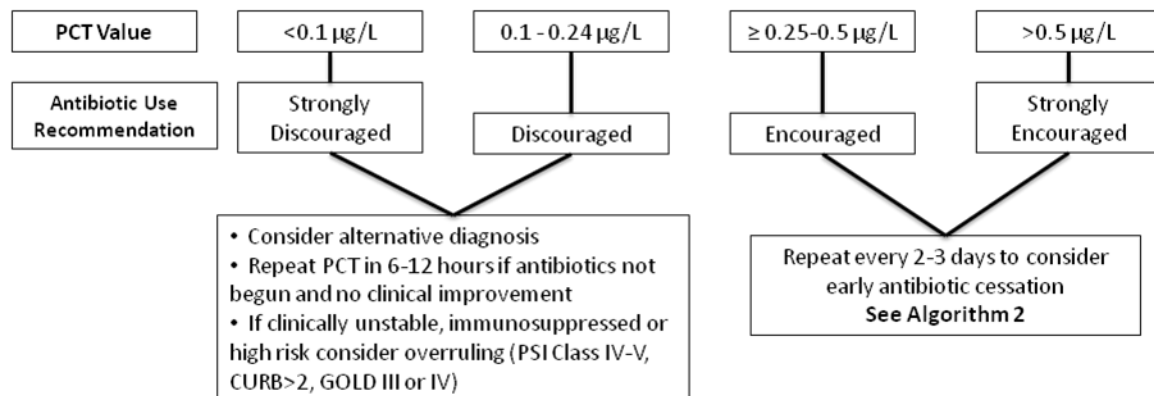
PROCALCITONIN:

Procalcitonin (PCT) a highly specific biomarker for systemic bacterial infection and has been shown to have significant utility in making decisions regarding antibiotic use in pneumonia. Excellent evidence supports the use of PCT for assisting clinicians in antibiotic management in LRTI including pneumonia, exacerbations of chronic bronchitis, and other assorted lower respiratory tract infections (bronchitis, asthma exacerbation, etc.). A meta-analysis of 8 studies with 3431 patients found the use of PCT in LRTI resulted in a 31% decrease in antibiotic prescriptions and a decrease in antibiotic duration of 1.3 days. Studies specifically addressing its use in pneumonia have had similar findings of decreased antibiotic use with equivalent clinical outcomes.

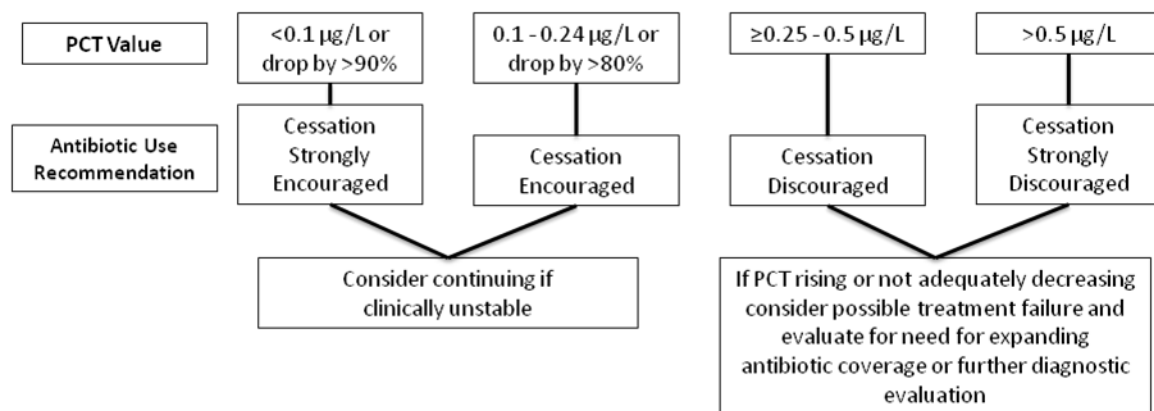
Procalcitonin can be used at The Nebraska Medical Center to assist clinicians in the diagnosis of infection and to support antimicrobial therapy decisions. **Decisions regarding antimicrobial therapy should NOT be based solely on procalcitonin serum concentrations;** procalcitonin should be placed into the clinical context of each patient scenario considering the site of possible infection, the likelihood of bacterial infection, the severity of illness, and any other pertinent clinical data.

It is suggested that patients considered at risk for pneumonia or being started on antibiotics for pneumonia have a PCT value measured on admission and every 2-3 days subsequently. Recommended interpretation of PCT values is listed below in **Algorithms 1 and 2**.

Algorithm 1: LRTI Initial PCT Value



Algorithm 2: LRTI PCT Value Follow Up



ANTIBIOTIC SELECTION:

The key decision in initial empiric therapy is whether the patient has risk factors for multidrug resistant (MDR) organisms (see above risk factors for MDR organisms table). Coverage in patients at risk for MDR pathogens should be directed at organisms such as *S. pneumoniae*, *S. aureus* (including MRSA), and gram-negative pathogens including *Pseudomonas aeruginosa*. The addition of a second antimicrobial agent can expand the empiric coverage for resistant Gram-negative pathogens. This combination therapy has been advocated by international consensus guidelines (Surviving Sepsis Campaign) in critically ill patients in severe sepsis or septic shock given delays to active therapy in this population has been associated with an increased mortality. Despite the clear mortality benefit of initially active therapy in critically ill patients, combination therapy remains controversial. The addition of a second agent has not been definitively associated with improved outcomes and depending on the severity of illness and patient population may be associated with worsened outcomes. Therefore, the addition of a second agent (e.g. tobramycin added to anti-pseudomonal beta-lactam) should be based on patient severity of illness, the likelihood of isolating resistant Gram-negative pathogens, and the potential adverse effects of additional therapy. De-escalation to a single active agent is **strongly** recommended when culture and susceptibility results return. Based on this we recommend clinicians weight the risk versus benefit and consider addition of a second agent in patients at particularly high risk for isolation of a resistant pathogen and those who are severely ill. When there is a concern for atypical pathogens such as *Legionella*, azithromycin should be added.

CONTINUATION OF THERAPY:

Broad-spectrum empiric antibiotic therapy should be accompanied by a commitment to de-escalate antibiotics, on the basis of serial clinical and microbiologic data, to limit the emergence of resistance and prevent toxicity.

All patients with HAP, VAP and HCAP should initially receive therapy intravenously, but conversion to oral/enteral therapy may be possible in certain responding patients. Clinical improvement usually becomes apparent after the first 48–72 hours of therapy, and therefore, the selected antimicrobial regimen should not generally be changed during this time unless progressive deterioration is noted or initial microbiologic studies so dictate. Clinical parameters including the white blood cell count, procalcitonin, and measures of oxygenation and core temperature have been used in several studies to define the normal pattern of resolution of pneumonia. The responding patient should have de-escalation of antibiotics, narrowing therapy to the most focused regimen possible on the basis of culture data.

The nonresponding patient should be evaluated for noninfectious mimics of pneumonia, unsuspected or drug-resistant organisms, extrapulmonary sites of infection, and complications of pneumonia and its therapy. Diagnostic testing should be directed to whichever of these causes is likely.

Efforts to reduce the duration of therapy are justified by studies of the natural history of the response to therapy. Data strongly support the premise that most patients with VAP, who receive appropriate antimicrobial therapy and have a good clinical response, can be treated with 7-8 days of antibiotics. Prolonged therapy leads to colonization with antibiotic resistant bacteria, which may precede a recurrent episode of VAP, increased toxicity, and increased cost. The exception to short courses of antibiotics is pneumonia due to non-lactose fermenting gram-negative rods (*Pseudomonas*, *Acinetobacter*, *Stenotrophomonas*) where a longer duration of treatment is recommended (10-14 days). Procalcitonin monitoring may also be useful in determining treatment duration where patients whose PCT values return to normal (<0.25) are candidates for stopping antimicrobials.

ALGORITHM:

