UW TASP Toolkit Module 1: Pneumonia

Theodore Wright, MD
January 2018

The following are abbreviated recommendations for treatment of community acquired pneumonia, Hospital acquired pneumonia, and ventilator associated pneumonia. For more in depth recommendations and guidelines please refer to the Infectious Disease Society of America/American Thoracic Society 2007 CAP guidelines and 2016 HAP/VAP guidelines.

Pneumonia occurs when the pulmonary parenchyma becomes infected. The cause of this condition can be varied; including viruses and bacteria. Often, patients are treated for pneumonia with antibiotics despite a non-bacterial etiology. This condition can arise in an outpatient or an inpatient setting. The etiology depends on the patient's underlying health, comorbidities, exposures, and place it was acquired. In deciding how to treat pneumonia appropriately it is important to consider the severity of the infection, patient comorbidities, the setting in which it began, and the setting in which you plan to treat it.

The incidence of pneumonia acquired in the community that requires hospitalization varies with age. When compared to adults aged 18-49 the incidence of pneumonia requiring hospitalization is 4,9, and 25 times higher for adults aged 50-64, 65-79, and > 80yo respectively (1). An infectious pathogen was isolated in only 38% of the cases requiring hospitalization. Viruses were found in 27% of cases and bacteria in only 14% (1). This underscores the significance of viral etiologies as a cause of pneumonia and the difficulty in finding a definitive explanation for the symptoms prompting admission.

Figure 1:

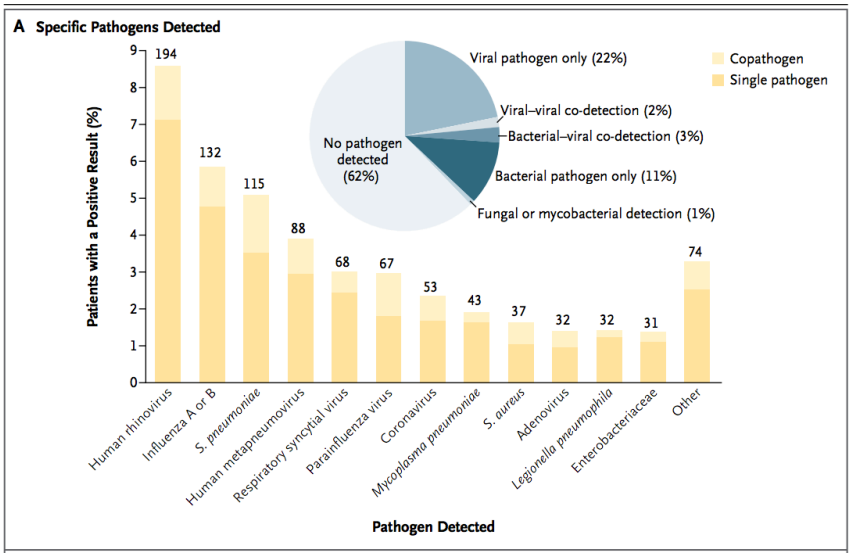

Figure 1- displays the specific pathogens found as a cause of pneumonia requiring hospitalization in the EPIC study 2010-2012 (1).

Figure 2:

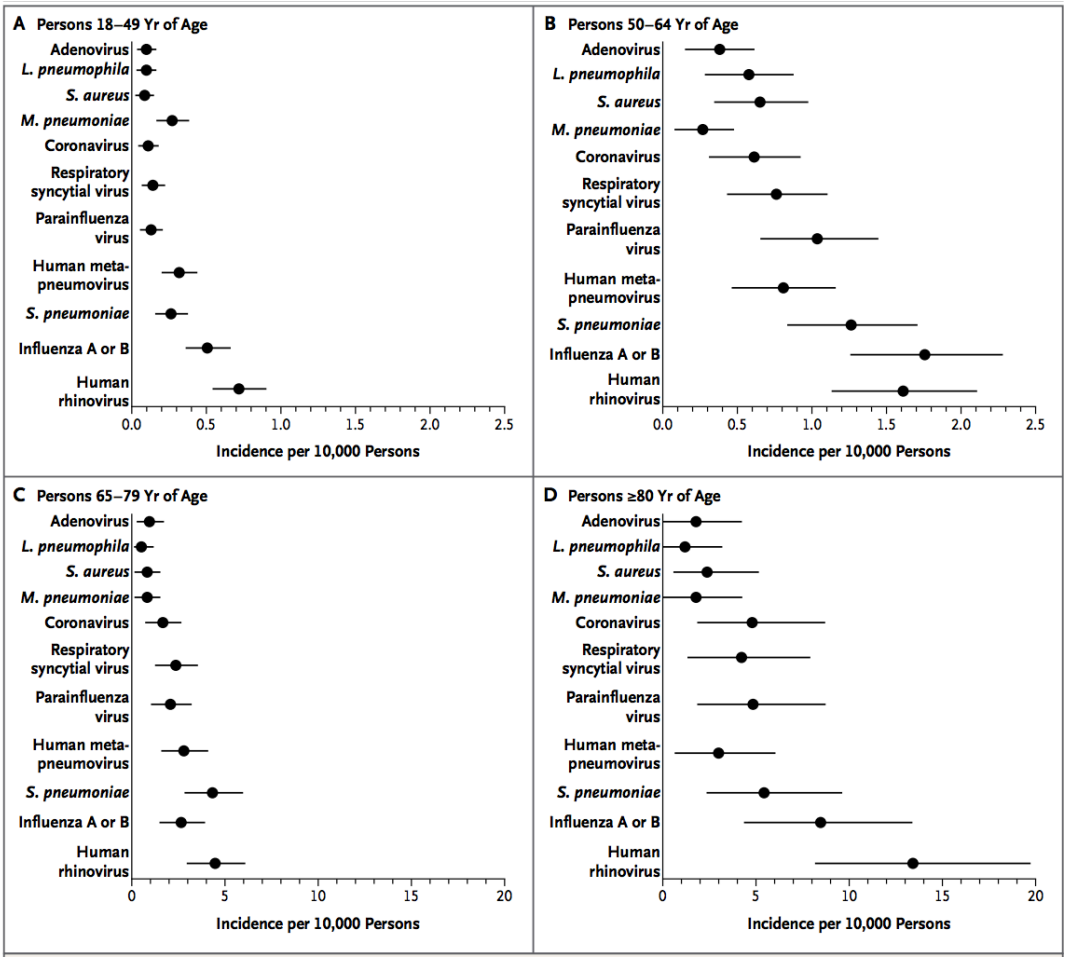

Figure 2 – Displays the specific pathogens found as a cause of pneumonia requiring hospitalization broken down by age. Published in the EPIC study 2010-2012 (1).

In patients who acquired pneumonia in the community and do not have a viral cause, the most common organisms responsible are *Streptococcus Pneumoniae* followed by *Staphylococcus Aureus*, *Mycoplasma Pneumoniae*, and *Legionella Pneumophila*. By far, the most common cause is *Streptoccus Pneumoniae*. Acquiring pneumonia while in the hospital may predispose you to other organisms, such as GNRs and multidrug resistant organisms. Previous IDSA guidelines have recommended empiric antimicrobials based on the setting in which they were acquired and the patient specific risk factors; Community acquired, healthcare associated, or hospital acquired. New guidelines for CAP are in progress and guidelines for HAP have recently been updated by the IDSA.

Healthcare Associated Pneumonia, HCAP, guidelines targeted empiric therapy for pneumonia towards GNRs and MDROs, that might be the cause of pneumonia in patients with other risk factors for pneumonia. The risk factors previously considered in recommendations for HCAP included: Hospitalization for >48 hours in the last 90 days, residence in a nursing home, home infusion therapy, chronic dialysis, home wound care, and a family member with a known resistant organism. These RF associated with HCAP focused on potential patient exposures, rather than patient comorbidities or functional status. A systematic review published in 2014 in CID pooled data from 24 studies of pneumonia and found that using the criteria for HCAP was unreliable at predicting mortality or those patients who would have an MDRO. The data found an alarmingly low sensitivity and specificity for using HCAP criteria to predict MDROs as a cause of pneumonia (2). These data confirmed the role of patient factors; such as recent antibiotics, comorbidities, and functional status, in determining your risk for an MDRO rather than simply your contact with the healthcare setting. For these reasons the new IDSA guidelines have eliminated the term HCAP.

Community acquired pneumonia can be treated in either the inpatient or outpatient setting. There are no specific criteria that requires a patient be treated in the hospital for pneumonia and if they are treated as an inpatient there is no requirement that they be treated with intravenous antibiotics. There are several protocols used to stratify a patient's risk and help guide healthcare providers in decisions to admit or discharge. The CURB-65 and Pneumonia Severity Index, PSI, are the most commonly used scores. Both scores have been validated and found to be equivalent (5).

Figure 3: CURB-65

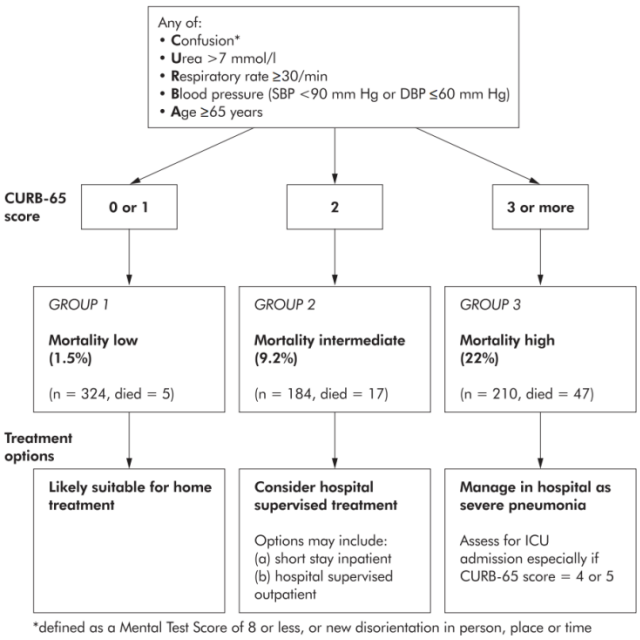

Figure 3 – Algorithm to assist in decision to admit patients with community Acquired Pneumonia (3).

Figure 4: Pneumonia Severity Index

TABLE 2. POINT SCORING SYSTEM FOR STEP 2 OF THE PREDICTION RULE FOR ASSIGNMENT TO RISK CLASSES II, III, IV, AND V.

CHARACTERISTIC	POINTS ASSIGNED*
Demographic factor	
Age	
Men	Age (yr)
Women	Age (yr) − 10
Nursing home resident	+10
Coexisting illnesses†	
Neoplastic disease	+30
Liver disease	+20
Congestive heart failure	+10
Cerebrovascular disease	+10
Renal disease	+10
Physical-examination findings	
Altered mental status‡	+20
Respiratory rate ≥30/min	+20
Systolic blood pressure <90 mm Hg	+20
Temperature <35°C or ≥40°C	+15
Pulse ≥125/min	+10
Laboratory and radiographic findings	
Arterial pH <7.35	+30
Blood urea nitrogen ≥30 mg/dl (11 mmol/liter)	+20
Sodium <130 mmol/liter	+20
Glucose ≥250 mg/dl (14 mmol/liter)	+10
Hematocrit <30%	+10
Partial pressure of arterial oxygen <60 mm Hg§	+10
Pleural effusion	+10

Figure 4 – PSI score to determine appropriate treatment setting for pneumonia. No risk factors is class I, score <70 is class II, score 71-90 is class II, score of 91-130 is class IV, and >130 is class V (4).

Patients with a CURB-65 score of 0 can be managed as outpatients. Patients with a CURB-65 score of 1 or 2 should be admitted to the hospital. Patients with a CURB-65 score of 3-5 should be admitted and considered for intensive care.

Patients with a PSI class I can be managed as outpatient. Patients with a PSI class II or III can be considered for home therapy but with home assistance. Patients who are PSI class IV or V should be admitted to the hospital and considered for intensive care.

The IDSA recommends treating patients with severe CAP in the ICU. Criteria for ICU admission for CAP include 1 of the following major criteria or 3 minor criteria.

Figure 5 – IDSA Criteria for ICU treatment of CAP. 1 Major criteria or 3 minor criteria are indications for ICU treatment of CAP.

Minor criteria[a]
Respiratory rate[b] ⩾30 breaths/min
PaO_2/FiO_2 ratio[b] ⩽250
Multilobar infiltrates
Confusion/disorientation
Uremia (BUN level, ⩾20 mg/dL)
Leukopenia[c] (WBC count, <4000 cells/mm^3)
Thrombocytopenia (platelet count, <100,000 cells/mm^3)
Hypothermia (core temperature, <36°C)
Hypotension requiring aggressive fluid resuscitation
Major criteria
Invasive mechanical ventilation
Septic shock with the need for vasopressors

NOTE. BUN, blood urea nitrogen; PaO_2/FiO_2, arterial oxygen pressure/fraction of inspired oxygen; WBC, white blood cell.

[a] Other criteria to consider include hypoglycemia (in nondiabetic patients), acute alcoholism/alcoholic withdrawal, hyponatremia, unexplained metabolic acidosis or elevated lactate level, cirrhosis, and asplenia.

[b] A need for noninvasive ventilation can substitute for a respiratory rate >30 breaths/min or a PaO_2/FiO_2 ratio <250.

[c] As a result of infection alone.

If a patient is diagnosed with CAP and does not require admission they can be treated as an outpatient with oral antibiotics targeting *streptococcus pneumoniae*; the preferred antibiotics are azithromycin 500 mg x 1 dose then 250 mg po daily x 4 days or doxycycline 100 mg po BID x 5 days. If the patient has risk factors for drug resistant streptococcus pneumoniae they should be treated with levofloxacin 750 mg PO daily or Amoxicillin 1000 mg PO TID plus azithromycin 500 mg PO x 1 dose then 250 mg PO daily x 4 days. Risk factors for drug resistant streptococcus pneumoniae include chronic heart disease, chronic lung disease, liver disease, or renal disease; diabetes mellitus, alcoholism, malignancy, asplenia, immunosuppression, or use of antimicrobials within the previous 3 months (6).

If a patient with CAP requires inpatient treatment then the first choice for antibiotics should be a beta lactam plus a macrolide; ceftriaxone 1 gm IV daily x 5 days plus azithromycin 500 mg PO/IV x 1 dose then 250 mg PO/IV daily x 4 days. Alternatives would include levofloxacin 750 mg PO/IV daily x 5 days. These antibiotics do not have to be IV. An oral option would include an oral beta lactam; such as amoxicillin 500 mg PO TID, or cefpodoxime 200 mg po Q12H, plus azithromycin.

A patient admitted with CAP who requires inpatient treatment in the ICU can be treated with a similar regimen as a non-ICU patient unless they are at risk for pseudomonas, or MDROs. The minimal regimen for ICU patients with pneumonia from the community would be a beta lactam plus azithromycin. For patients felt to be at risk for *pseudomonas aeruginosa* pneumonia the initial treatment should include piperacillin-tazobactam 4.5 gm IV Q6H or meropenem 1 gm IV Q8H plus either levofloxacin 750 mg IV/PO daily or ciprofloxacin 400 mg IV/PO BID.

If a patient is started on intravenous therapy for CAP they should be switched to oral therapy once they are hemodynamically stable, clinically improving, and able to take oral medications. It is not necessary to observe a patient in the hospital after changing to orals if they are

otherwise ready for discharge. Even in the case of pneumococcal bacteremia it is safe to switch to oral therapy once the patient is clinically stable, afebrile, and able to take oral medications.

Antibiotics should be switched to orals after 48-72 hours of no fever and no more than 1 sign of clinical instability. Signs of clinical instability include T >37.8C, HR >100 bpm, RR >24, SBP <90 mmHg, SaO2 < 90% or pO2 < 60 mmHg on room air, inability to maintain oral intake, abnormal mental status. A longer duration is helpful if the initial therapy was not active against an identified organism or if the course was complicated by an extra-pulmonary infection. Oral options for patients initially treated with an IV beta lactam and a macrolide who have no concern for drug resistant streptococcus pneumoniae can be switched to amoxicillin 500 mg po TID or 875 mg PO BID. If the patient has already received 1.5 gm of azithromycin this can be discontinued. Other options for patients without risk factors for drug resistant streptococcus pneumoniae include azithromycin 500 mg po daily, clarithromycin 500 mg po BID, or doxycycline 100 mg po BID.

Risk factors for drug resistant *streptococcus pneumoniae* include age >65 yo; beta-lactam, macrolide, or fluoroquinolone therapy within the past three to six months, alcoholism, medical comorbidities, immunosuppressive therapy, or exposure to a child in a daycare center. If a patient has risk factors for drug resistant *streptococcus pneumoniae* then they can be changed to high dose amoxicillin 1 gm PO TID (6).

The diagnosis of HAP should be made off clinical presentation and non-invasive sputum sampling; such as expectorated sputum. When possible antibiotic therapy for HAP should be based of microbiological data.

The empiric regimen for the treatment of HAP can include coverage for MDROs, including MRSA and GNRs. Without risk factors for MRSA the preferred empiric coverage is cefepime 2 gm IV Q8H. Other options include piperacillin-tazobactam 4.5 gm IV Q6H, levofloxacin 750 mg IV Qday, imipenem 500 mg IV Q6H, meropenem 1 gm IV Q8H. If the patient has risk factors for MRSA then vancomycin 15 mg/kg IV Q8H-Q12H or linezolid 600 mg IVQ12H should be added. Vancomycin is preferred over linezolid. Consider a loading dose of vancomycin 25-30 mg/kg IV x 1, not to exceed 2 gm. If the patient is at high risk of mortality and received IV antibiotics in the last 90 days then the preferred empiric regimen is 2 of the following, avoid 2 beta lactams: piperacillin-Tazobactam 4.5 gm IV Q6H, cefepime or ceftazidime 2 gm IV Q6H, levofloxacin 750 mg IV Qday, ciprofloxacin 400 mg IV Q8H, imipenem 500 mg IV Q6H, meropenem 1 gm IV Q8H, amikacin 15-20 mg/kg IV QDay, gentamicin 5-7 mg/kg IV Qday, tobramycin 5-7 mg/kg IV Qday or aztreonam 2 gm IV Q8H, plus add vancomycin 15 mg/kg IV Q8H-Q12H with goal trough 15-20 mg/mL and consider a loading dose of 25-30 mg/kg IV x 1. A second line option for MRSA is Linezolid 600 mg IV Q12H.

Figure 6:

Table 4. Recommended Initial Empiric Antibiotic Therapy for Hospital-Acquired Pneumonia (Non-Ventilator-Associated Pneumonia)

Not at High Risk of Mortality[a] and no Factors Increasing the Likelihood of MRSA[b,c]	Not at High Risk of Mortality[a] but With Factors Increasing the Likelihood of MRSA[b,c]	High Risk of Mortality or Receipt of Intravenous Antibiotics During the Prior 90 d[b,c]
One of the following:	One of the following:	Two of the following, avoid β-lactams:
Piperacillin-tazobactam[d] 4.5 g IV q6h	Piperacillin-tazobactam[d] 4.5 g IV q6h	Piperacillin-tazobactam[d] 4.5 g IV q6h
OR	OR	OR
Cefepime[d] 2 g IV q8h	Cefepime[d] or ceftazidime[d] 2 g IV q8h	Cefepime[d] or ceftazidime[d] 2 g IV q8h
OR	OR	OR
Levofloxacin 750 mg IV daily	Levofloxacin 750 mg IV daily	Levofloxacin 750 mg IV daily
	Ciprofloxacin 400 mg IV q8h	Ciprofloxacin 400 mg IV q8h
	OR	OR
Imipenem[d] 500 mg IV q6h	Imipenem[d] 500 mg IV q6h	Imipenem[d] 500 mg IV q6h
Meropenem[d] 1 g IV q8h	Meropenem[d] 1 g IV q8h	Meropenem[d] 1 g IV q8h
	OR	OR
	Aztreonam 2 g IV q8h	Amikacin 15–20 mg/kg IV daily
		Gentamicin 5–7 mg/kg IV daily
		Tobramycin 5–7 mg/kg IV daily
		OR
		Aztreonam[e] 2 g IV q8h
	Plus: Vancomycin 15 mg/kg IV q8–12h with goal to target 15–20 mg/mL trough level (consider a loading dose of 25–30 mg/kg × 1 for severe illness)	Plus: Vancomycin 15 mg/kg IV q8–12h with goal to target 15–20 mg/mL trough level (consider a loading dose of 25–30 mg/kg IV × 1 for severe illness)
	OR	OR
	Linezolid 600 mg IV q12h	Linezolid 600 mg IV q12h
		If MRSA coverage is not going to be used, include coverage for MSSA. Options include: Piperacillin-tazobactam, cefepime, levofloxacin, imipenem, meropenem. Oxacillin, nafcillin, and cefazolin are preferred for the treatment of proven MSSA, but would ordinarily not be used in an empiric regimen for HAP.
If patient has severe penicillin allergy and aztreonam is going to be used instead of any β-lactam–based antibiotic, include coverage for MSSA.		

Abbreviations: HAP, hospital-acquired pneumonia; IV, intravenous; MRSA, methicillin-resistant Staphylococcus aureus; MSSA, methicillin-sensitive Staphylococcus aureus.

Figure 6 – IDSA/ATS Recommended empiric therapy for HAP (7).

The IDSA/ATS recommends diagnosing VAP based off clinical presentation, imaging, and non-invasive sampling. Non-invasive sampling includes tracheal aspiration, but not bronchoalveolar lavage or bronchial brush.

Empiric treatment of VAP should include coverage for MSSA, GNR, and *Pseudomonas Aeruginosa*, in addition to the organisms covered by a typical CAP antibiotic regimen. If your hospital's rates of MRSA are >10-20% or the patient is known to be colonized with MRSA then coverage for MRSA should be included. Empiric treatment for MRSA should be vancomycin, and a second option would be linezolid. Do not use daptomycin to treat pneumonia. Empiric options for VAP in a patient requiring MRSA coverage include Vancomycin 15 mg/kg IV Q8H-Q12H (consider a 25-30 mg/kg loading dose for severe illness, not to exceed 2 gm) plus piperacillin-tazobactam 4.5 gm IV Q6H or cefepime 2 gm IV Q8H. Cefepime is preferred over piperacillin-tazobactam. IDSA recommends alternatives; including ceftazidime 2 gm IV Q8H, imipenem 500mg IV Q6H, meropenem 1 gm IV Q8H, or aztreonam 2 gm IV Q8H. We do not recommend these alternatives without ID consultation. Two indications for double coverage of pseudomonas are when you do not yet have sensitivities or you have sensitivities and the patient is still severely ill. Double coverage for pseudomonas is typically achieved by adding Ciprofloxacin 400mg IV Q8H or levofloxacin 750 mg IV Q24H. Other less desirable options for double coverage of pseudomonas include gentamicin 5-7 mg/kg IV Q24H, amikacin 15-20 mg/kg IV Q24H, tobramycin 5-7 mg/kg IV Q24H, colistin 5 mg/kg IV x 1 loading dose then 2.5 mg IV Q12H thereafter, or polymyxin B 2.5-3.0 mg/kg d divided in 2 daily IV doses. These

second line treatment options for pseudomonas are associated with more adverse events and should be used with ID consultation.

Pseudomonas should be treated with 2 anti-pseudomonal antibiotics if the patient is severely ill or if sensitivities are pending and the patient has risk factors for MDRO. These risk factors include prior IV antibiotics in the last 90 days, sepsis at time of VAP, ARDS preceding VAP, 5 or more days of hospitalization prior to onset of VAP, dialysis. The risk factors for MDR HAP include prior IV antibiotic use in the last 90 days. Risk factors for MRSA VAP/HAP include prior IV antibiotics in the last 90 days. The risk factors for MDR pseudomonas VAP/HAP also includes IV antibiotics in the last 90 days.

Figure 7:

Table 3. Suggested Empiric Treatment Options for Clinically Suspected Ventilator-Associated Pneumonia in Units Where Empiric Methicillin-Resistant *Staphylococcus aureus* Coverage and Double Antipseudomonal/Gram-Negative Coverage Are Appropriate

A. Gram-Positive Antibiotics With MRSA Activity	B. Gram-Negative Antibiotics With Antipseudomonal Activity: β-Lactam–Based Agents	C. Gram-Negative Antibiotics With Antipseudomonal Activity: Non-β-Lactam–Based Agents
Glycopeptides[a] Vancomycin 15 mg/kg IV q8–12h (consider a loading dose of 25–30 mg/kg × 1 for severe illness)	Antipseudomonal penicillins[b] Piperacillin-tazobactam 4.5 g IV q6h[b]	Fluoroquinolones Ciprofloxacin 400 mg IV q8h Levofloxacin 750 mg IV q24h
OR	OR	OR
Oxazolidinones Linezolid 600 mg IV q12h	Cephalosporins[b] Cefepime 2 g IV q8h Ceftazidime 2 g IV q8h	Aminoglycosides[a,c] Amikacin 15–20 mg/kg IV q24h Gentamicin 5–7 mg/kg IV q24h Tobramycin 5–7 mg/kg IV q24h
	OR	OR
	Carbapenems[b] Imipenem 500 mg IV q6h[d] Meropenem 1 g IV q8h	Polymyxins[a,e] Colistin 5 mg/kg IV × 1 (loading dose) followed by 2.5 mg × (1.5 × CrCl + 30) IV q12h (maintenance dose) [135] Polymyxin B 2.5–3.0 mg/kg/d divided in 2 daily IV doses
	OR	
	Monobactams[f] Aztreonam 2 g IV q8h	

Figure 7 – IDSA/ATS Recommended empiric therapy for suspected VAP when MRSA coverage is indicated (7).

Duration of therapy for HAP and VAP should be 7 days total. This therapy may need to be extended depending on patient condition and response to therapy. When possible, based on microbiological data and after clinical improvement a patient's antibiotics should be switched to an oral therapy.

Efforts should be made to standardize your institution's prescribing habits and reduce inappropriate antibiotic use. One way to do this is to create evidence-based standard order sets for common infections requiring admission. An example of such order set for pneumonia:

- Patient meets admission criteria for community acquired pneumonia, CAP, and does not require intensive care unit:
    - Ceftriaxone 1 gm IV Q24H plus Azithromycin 500 mg IV/PO Q24H.
    - If PCN allergic:
        - Levofloxacin 750 mg po/IV day.
- De-escalating to oral abx for CAP:
    - No RF for drug resistant strep pneumo – Pick one of the following
        - Amoxicillin 500 mg po TID or 875 mg po BID.
        - Doxycycline 100 mg po BID
    - Okay to stop azithro if the patient has received 1.5 gm.
    - If RF for drug resistant strep pneumo (age >65 yo; beta-lactam, macrolide, of fluoroquinolone therapy within the past three to six months, alcoholism, medical comorbidities, immunosuppressive therapy, or exposure to a child in a daycare center) – Please use the following
        - Amoxicillin 1gm PO TID
        - If PCN allergic:
            - Levofloxacin 750 mg po daily
- Patient develops pneumonia >48 hours after admission to the hospital and no signs or symptoms of pneumonia were present on admission.
    - Patient has no RF for MRSA and no known MRSA colonization and you hospital has < 10-20% prevalence of MRSA. Choose one of the following:
        - Cefepime 2 gm IV Q8H – Preferred
        - Piperacillin-tazobactam 4.5 gm IV Q6H.
        - Levofloxacin 750 mg IV/PO daily.
        - Meropenem 1 gm IV Q8H
    - Patient has RF for MRSA or known MRSA colonization or your hospital has > 10-20% prevalence of MRSA.
        - One of the following:
            - Vancomycin 25-30 mg/kg IV x 1 followed by 15 mg/kg IV Q8H-Q12H mg/kg IV with goal trough 10-20
            - Linezolid 600 mg IV/PO Q12H
        - Plus one of the following
            - Cefepime 2 gm IV Q8H – Preferred
            - Piperacillin-tazobactam 4.5 gm IV Q6H
            - Levofloxacin 750 mg IV/PO daily
            - Meropenem 1 gm IV Q8H

    - If the patient has a high risk of mortality and received IV abx in the last 90 days then please prescribe 2 of the following; avoiding two from the same class:
        - Cefepime 2 gm IV Q8H
        - Ceftazidime 2 gm IV Q8H
        - Piperacillin-Tazobactam 4.5gm IV Q6H
        - Levofloxacin 750 mg po/IV daily
        - Cipro 400 mg IV/PO daily
        - Gentamicin 5-7 ,mg/kg IV Qday
        - Aztreonam 2 gm IV Q8H
- Patient develops pneumonia 48-72 hours after intubation – Empiric therapy should cover MSSA, GNR, and *Pseudomonas Aeruginosa:*
    - If no RF for MRSA and your hospital has < 10-20% prevalence of MRSA then please start one of the following:
        - Cefepime 2 gm IV Q8H – Preferred
        - Piperacillin-Tazobactam 4.5 gm IV Q6H
        - Ceftazidime 2 gm IV Q8H
        - Meropenem 1 gm IV Q8H
        - Aztreonam 2 gm IV Q8H
    - If your patient has RF for MRSA or known colonization with MRSA or your hospital has a MRSA prevalence >10-20% then please also add one of the following:
        - Vancomycin 25-30 mg/kg loading dose followed by 15-20 mg/kg IV Q8H to Q12H - Preferred.
        - Linezolid 600 mg IV Q12H.
    - If you are awaiting culture results for a critically ill patient or your patient has known Pseudomonas Aeruginosa and is failing to improve on a single agent that is known to be susceptible to then consider adding a second agent from the following classes without using two antibiotics from the same class:
        - Ciprofloxacin 400 mg IV Q8H
        - Levofloxacin 750 mg IV Qday
        - Gentamicin 5-7 mg/kg IV Q24H

References:

1. Jain, S.; et al. “Community Acquired Pneumonia Requiring Hospitalization among US Adults.” NEJM. 373:5. July 30,2015.
2. Chalmers, JD; Rother, Catriona; Salih, W; Ewig, S. “Healthcare-Associated Pneumonia Does Not Accurately Identify Potentially Resistant Organisms: A Systematic Review and Meta-Analaysis.” CID. 2014:58.
3. Lim, WS; et al. “Defining Community Acquired Pneumonia Severity on Presentation to Hospital: An International Derivation and Validation Study.” Thorax. 2003. Vol 58.

4. Fine, MJ; et al. “A Prediction Rule To Identify Low Risk Patients with Community Acquired Pneumonia.” NEJM. 1999. 336(4).
5. Chalmers, JD; et al. “Severity Assessment Tools for Predicting Mortality in Hospitalized Patients with Community-Acquired Pneumonia. Systematic Review and Meta-Analysis.” Thorax. 2010. Vol 65.
6. Mandell, LA; et al. “IDSA/ATS Consensus Guidelines on the Management of Community-Acquired Pneumonia in Adults.” CID. 2007. Vol 44.
7. Kalil, A.C.; Et Al. “Management of Adults with Hospital-Acquired and Ventilator-Associated Pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society.” CID. 2016. Vol 63.