PNEUMONIA REVIEW - 2024

DIAGNOSIS

Chest infiltrates and clinical symptoms

The diagnosis of PNA requires demonstration of a new lung infiltrate plus clinical evidence that the infiltrate is of infectious origin

- Chest imaging infiltrates
    - CXR infiltrates are present in most patients (93% to 97%)
    - CT chest is required in some patients
        - High suspicion of PNA with negative CXR particularly in those with immunocompromised status
        - To identify complications such as necrotizing PNA, abscess, parapneumonic effusions, or empyema
        - To assess alternate or concurrent diagnosis
        - To assess lack of response to treatment
- Clinical compatible syndrome includes the new onset of fever, cough, leukocytosis, and decline in oxygenation

Procalcitonin

PCT level is not necessary for the diagnosis of PNA but is generally recommended at the time of diagnosis and serially thereafter to help guide antibiotic de-escalation on case-by-case analysis.

- Levels of less than 0.5 µg/L or levels that decrease by greater than or equal to 80% from peak levels may guide antibiotic discontinuation once patients stabilize

The use of PCT-guided antibiotic initiation and/or discontinuation for infections should be used with caution because:

- Certain non-infectious conditions have been found to have elevated PCT levels at baseline including:
    - Severe acute or chronic renal dysfunction
    - Major recent surgery or trauma
    - Shock or post-cardiac arrest
    - Severe pancreatitis
    - Hematologic malignancies
    - Acetaminophen overdose
- Absent of elevated PCT does not exclude PNA, therefore, in patients with clinical suspicion of PNA and normal PCT, clinicians should not initially withhold antibiotics.

DEFINTION AND CLASSIFICATION

By site of acquisition:

- **Community-acquired pneumonia** (CAP) refers to an acute infection of the pulmonary parenchyma acquired outside of the hospital.
- **Hospital acquired pneumonia (HAP)** refers to an acute infection of the pulmonary parenchyma acquired in the hospital settings and encompasses both **non-ventilator hospital-acquired pneumonia (nvHAP) and ventilator-associated pneumonia (VAP).**

- **nvHAP** refers to pneumonia (PNA) acquired ≥48 hours after hospital admission not on ventilator.
- **VAP** refers to PNA acquired ≥48 hours after endotracheal intubation.

By etiology:

- Typical PNA
- Atypical PNA
- Aspiration PNA
- Chemical pneumonitis

By severity:

- Determining the severity of PNA is based on clinical judgement supplemented by using available severity scores. The most commonly used are the American Thoracic Society (ATS)/Infectious Diseases Society of America (IDSA) criteria and the Pneumonia Severity Index (PSI) - available at MDCalc.
- **Severe PNA** is defined by 1 major criteria or ≥3 minor ATS/IDSA) criteria or PSI score >130

ATS/IDSA severity criteria

- Presence of **1 major** criterion or **≥3minor** criteria
  - Major criteria
    - Respiratory failure requiring mechanical ventilation
    - Sepsis requiring vasopressor support
  - Minor criteria
    - Altered mental status
    - Hypotension requiring fluid support
    - Temperature <36°C (96.8°F)
    - Respiratory rate ≥30 breaths/minute
    - Hypoxemia with PaO_2/FiO_2 ratio ≤250
    - BUN ≥20 mg/dL
    - Leukocyte count <4000
    - Platelet count <100,000
    - Multi-lobar infiltrates

	PSI score	Risk class	Mortality risk
PNA severity			
Mild	≤70	I - II	Low
Moderate	71-90	III	Low
	91-130	IV	Moderate
Severe	>130	V	High

ETIOLOGY

Community-acquired pneumonia (CAP)

The most common CAP pathogens include:

- Respiratory viruses (rhinovirus, influenza, covid, and other respiratory viruses such as parainfluenza, respiratory syncytial virus, and human metapneumovirus)
- Typical bacteria (Streptococcus pneumoniae, Haemophilus influenzae, Moraxella catarrhalis)
- Atypical bacteria (Legionella spp., Mycoplasma pneumoniae, Chlamydia pneumonia)
- Oropharyngeal aerobes and anaerobes in the setting of aspiration

Pseudomonas and methicillin-resistant Staphylococcus aureus (MRSA) are less common causes and predominantly occur in patients with specific risk factors.

Hospital-acquired pneumonia (HAP)
The most common organisms for HAP include:

- MRSA and *Pseudomonas aeruginosa*
- Other common causes include other aerobic gram-negative bacilli (e.g., Escherichia coli, Klebsiella pneumoniae, Enterobacter spp., Acinetobacter spp.) and gram-positive cocci (e.g., Streptococcus spp.)

Aspiration-chemical pneumonitis and PNA

- Pathogens have shifted from anaerobes to aerobes

MICROBIOLOGY TESTING
The benefit of obtaining a microbiologic diagnosis should be balanced against the time and cost associated with an extensive evaluation in each patient.

Pretreatment Gram stain and culture of respiratory secretions or blood cultures in adults with CAP managed in the hospital setting are only indicated in patients with moderate to severe CAP or with risk factors for Pseudomonas, multi drug resistant (MDR) pathogens, or MRSA.

Urine testing for pneumococcal and Legionella antigens in adults with CAP are only indicated for patients with severe PNA and legionella for those with occupational (gardening) or epidemiologic risk factors

A tiered approach based on PNA severity, and the site of care is generally recommended.

Mild PNA – does not require admission related to the PNA

- Microbiologic testing is not needed
    - Empiric antibiotic therapy is generally successful, and knowledge of the infecting pathogen does not usually improve outcomes

Moderate PNA – generally requires non-ICU admission

- Blood cultures if risk factors for Pseudomonas, MDR pathogens, or MRSA
- Sputum Gram stain and culture if risk factors for Pseudomonas, MDR pathogens, or MRSA
- Legionella spp antigen if occupational (gardening) or epidemiologic risk factors or underlying conditions such as immunocompromise status, elderly, and smoker patients
    - PCR when available, urinary antigen test as an alternative
        - PCR on sputum sample is preferred for the diagnosis of Legionella spp. because it detects the most clinically relevant Legionella spp.

        - The urine antigen test is an acceptable alternative when PCR is not available but is specific for Legionella pneumophila serogroup 1
- COVID-19 and influenza PCR testing
    - Result would change management
- Other PCR tests are conditional
    - PNA PCR panel is generally recommended only for severe PNA or for immunocompromised patients*
    - Respiratory PCR viral panel
        - Usually not required
            - In case-by-case analysis can be useful in patients with negative COVID-19 and influenza PCR testing

Severe PNA – requires ICU admission

- Blood cultures
- Sputum Gram stain and culture
- Sputum or BAL PNA panel
- Tuberculosis, fungal pathogens, and Nocardia testing for patients with cavitary PNA
- Opportunistic pathogens such as Pneumocystis jirovecii, fungal pathogens, parasites, and less common viral pathogens such as cytomegalovirus for immunocompromised patients
- Galactomannan or β-D-glucan for patients with suspected invasive pulmonary aspergillosis (IPA) or invasive candidiasis
    - Patients with CT chest findings consistent with IPA or invasive candidiasis associated with either:
        - Immunosuppression particularly with neutropenia, or
        - Underlying conditions such as prolonged steroid therapy, COPD, cirrhosis, malnutrition, parenteral nutrition, severe influenza or COVID-19 infection, even in the absence of severe immunosuppression

*Immunocompromise criteria

- Neutropenia
- Undergoing active cancer therapy
- History of solid-organ or blood component transplantation
- Advanced HIV disease
- History of chronic use of immunosuppressive medications, including systemic corticosteroids
    - Usual steroid dose considered clinically relevant is prednisone or its equivalent ≥20 mg/d longer than ≥3 weeks
    - If steroids are used combined with other immunosppresant, lower doses are relevant

PCR tests available at UF Health Flagler Hospital

- **Respiratory Quad -** includes COVID-19, influenza A and B, and RSV
- **Respiratory film array panel -** includes 4-Plex and other viruses such as adenovirus, parainfluenza, and human metapneumovirus
- **PNA panel** includes respiratory Quad and film array plus typical and atypical bacteria along with antimicrobial resistance

    - KPC: carbapenemases
    - CTX-M: ESBL
    - mecA/C and MREJ: MRSA

PCR tests results must be interpreted with caution:

- The detection of single viral pathogen does not confirm the diagnosis of isolated viral PNA because viruses can serve as cofactors in the pathogenesis of bacterial PNA
- Viruses and bacteria can be harbored asymptomatically

TREATMENT

Determining whether a patient with PNA can be safely treated as an outpatient or requires admission to an observation unit, general medical floor, or ICU, is an essential first step.

- Along with clinical judgement, severity of illness is the most critical factor in making this determination, but other factors should also be considered
- For patients not requiring vasopressors or mechanical ventilator support using the IDSA/ATS minor severity criteria and the PSI score together with clinical judgment should guide the need for higher levels of treatment intensity

The three levels of severity (mild, moderate, and severe) generally correspond to three levels of care:

Mild PNA (PSI score ≤70)

- Patients who are otherwise healthy with normal vital signs (apart from fever) and no concern for complications can be managed in the outpatient setting

Moderate and severe PNA (PSI score >70)

- Should be admitted with early administration of appropriate antibiotics to improve outcomes
    - Those with *severe PNA* should be admitted to the ICU
    - Those with *moderate PNA* with PSI 71-90 (low risk mortality) can be considered to be managed in the outpatient setting

ANTIBIOTIC THERAPY

Start antibiotics as soon as PNA is the appropriate working diagnosis

- Within four hours of presentation for inpatients and within one hour for those who are critically ill

Because of the high mortality associated with severe PNA and uncertainty of adequate gastrointestinal absorption of oral antibiotics in severely ill patients, antibiotics should be administered IV at the start of therapy.

The selection of an empiric antibiotic regimen is based on the severity of illness, site of care, most likely pathogens, the likelihood of infection with multidrug-resistant (MDR) pathogens or Pseudomonas, or MRSA, and patient drug allergy or intolerance. The Drug Resistance in Pneumonia (DRIP) score can be used to predict risk for community-acquired pneumonia due to drug-resistant pathogens.

Risk factors for Pseudomonas or MDR pathogens

- Strong - patients with these risk factors generally require treatment with an empiric regimen that includes coverage for these organisms
    - Known colonization or past infection with these organisms
    - Detection of gram-negative rods on a good-quality sputum Gram stain
    - Hospitalization with receipt of IV antibiotics in the prior 3 months
- Other risk factors that should raise suspicion
    - Recent hospitalization or stay in a long-term care facility
    - Recent antibiotic use of any kind
    - Frequent COPD exacerbations requiring glucocorticoid and/or antibiotic use
    - Structural lung diseases (e.g., bronchiectasis, cystic fibrosis)
    - Presence of multiple medical comorbidities (e.g., chronic heart, lung, kidney, liver disease, diabetes mellitus, alcoholism)
    - Immunosuppression

Risk factors for MRSA

- Strong - patients with these risk factors generally require treatment with an empiric regimen that includes MRSA coverage
    - Known MRSA colonization
    - Prior MRSA infection
    - Detection of gram-positive cocci in clusters on a good-quality sputum Gram stain
- Other risk factors that should raise suspicion
    - Recent hospitalization particularly with receipt of intravenous antibiotics within the prior three months
    - Recent influenza-like illness
    - Necrotizing or cavitary pneumonia
    - Empyema
    - Immunosuppression
    - Risk factors for MRSA colonization
        - End-stage kidney disease
        - Crowded living conditions (e.g., incarceration)
        - Injection drug use
        - Contact sports participation
        - Men who have sex with men

- In all patients treated empirically for MRSA PNA, a rapid nasal PCR should be obtained to help guide subsequent therapy
    - For those who are stable or improving with negative PCR and/or sputum Gram stain results, MRSA coverage can generally be discontinued

Risk factors associated with increased mortality in patients with VAP

- Septic shock at the time of VAP
- ARDS preceding VAP
- ≥5 days of hospitalization prior to the occurrence of VAP
- Acute renal replacement therapy prior to VAP onset

Antibiotics recommended doses

- Oral amoxicillin 1 g every 8 hours
- Oral amoxicillin-clavulanate 875 mg every 12 hours
- Ampicillin-sulbactam 3 g IV every 6 hours
- Macrolides
    - Azithromycin 500 mg orally or IV daily
- Doxycycline 100 mg orally or IV every 12 hours
- Oral third-generation cephalosporins
    - Cefdinir 300 mg every 12 hours
    - Cefpodoxime 200 mg every 12 hours
- IV third-fourth generation cephalosporins
    - Ceftriaxone 1 to 2 g IV daily
    - Cefepime 2g IV every 8 hours
    - Cefotaxime1 to 2 g IV every 8 hours
    - Ceftaroline 600 mg IV every 12 hours
- Respiratory fluoroquinolones
    - Levofloxacin 750 mg IV or orally daily
    - Ciprofloxacin 400 every 8 hours or 750 mg IV or orally every12 hours (depending on severity)
    - Moxifloxacin 400 mg orally daily
- Piperacillin-tazobactam 4.5 g every 6 hours
    - For critically ill patients extended-4h IV continuous infusion after the initial loading dose is preferred)
- Vancomycin loading dose 15-20 mg/Kg IV with interval adjustments based on AUC (preferred) or MIC, and renal function
- Linezolid 600 mg IV every 12 hours
- Aztreonam 2 gr IV every 8 hours
- Carbapenems
    - For critically ill patients extended-4h IV continuous infusion after the initial loading dose is preferred)
        - Meropenem 1 gr IV every 8 hours
        - Ertapenem 1 gr IV daily (does not cover Pseudomonas)
- Metronidazole 500 mg IV every 8 hours IV or orally
- Aminoglycosides
    - Tobramycin
        - Systemic: 5 -7 mg/Kg/dose IV daily
        - Inhaled: 300 mg by nebulization every 12 hours x7 days
    - Amikacin
        - Systemic 15-20 mg/Kg/dose IV daily
        - Inhaled 400 mg every 12 hours or 20 mg/Kg IBW by nebulization daily x7 days
- Inhaled colistin: three nebulizations of 5 million IU can be administered/24 h

INITIAL EMPIRIC ANTIBIOTIC SELECTION FOR CAP *(ATS and IDSA 2019 recommendations)*

Patients with CAP not requiring admission

- For most patients aged <65 years who are otherwise healthy and have not recently used antibiotics
    - Oral amoxicillin plus either a macrolide (preferred) or doxycycline
- For patients who have major comorbidities (e.g., chronic heart, lung, kidney, or liver disease, diabetes mellitus, alcohol dependence, immunosuppression), smokers, and/or who have used antibiotics within the past three months
    - Oral amoxicillin-clavulanate plus either a macrolide (preferred) or doxycycline
    - Alternative regimen
        - Oral third-generation cephalosporin (e.g., cefdinir or cefpodoxime) plus either a macrolide (preferred) or doxycycline
- For patients who cannot use any beta-lactam or with structural lung disease (e.g., bronchiectasis, cystic fibrosis)
    - Oral fluoroquinolone because its spectrum of activity includes Enterobacteriaceae
    - Alternative regimen
        - Omadacycline, newer tetracycline agent that is active against most CAP pathogens, including Enterobacteriaceae can be considered for patients who cannot tolerate beta-lactams (or other agents) and want to avoid fluoroquinolones

Patients with CAP requiring non-ICU admission

- *Without risk factors for Pseudomonas or MDR pathogens*
    - Intravenous combination with an antipneumococcal beta-lactam plus a macrolide
        - Ceftriaxone or cefotaxime or ampicillin-sulbactam

    AND

        - Azithromycin or doxycycline
    - Alternative regimen
        - Monotherapy with a respiratory fluoroquinolone
            - The risk of selection for resistance in colonizing organisms are generally thought to be greater with fluoroquinolones than with the combination therapy regimens

- *With risk factors for Pseudomonas or MDR pathogens*
    - Combination therapy with an antipseudomonal/antipneumococcal beta-lactam and an antipseudomonal fluoroquinolone
        - Piperacillin-tazobactam or cefepime plus levofloxacin or ciprofloxacin

- *With risk factors for MRSA*
    - Add vancomycin or linezolid

- *For patients with beta-lactam allergy*
    - Without risk factors for Pseudomonas or MDR pathogens
        - Monotherapy with respiratory fluoroquinolone
    - With risk factors for Pseudomonas or MDR pathogens
        - Aztreonam plus respiratory fluoroquinolone

Patients with CAP admitted to the ICU

- *Without risk factors for Pseudomonas or MDR pathogens*
    - Treatment is similar to patients not requiring ICU except that monotherapy or oral antibiotics are not recommended
        - Beta-lactam plus either a macrolide (preferred) or doxycycline, or
        - Beta-lactam plus a respiratory fluoroquinolone
        - For patients with MRSA risk factors add either vancomycin or linezolid
        - For patients with beta-lactam allergy monotherapy with respiratory fluoroquinolone

- *With risk factors for Pseudomonas or MDR pathogens*
    - Combination therapy with an antipseudomonal/antipneumococcal beta-lactam antibiotic and an antipseudomonal fluoroquinolone
        - Antipseudomonal beta-lactam
            - Piperacillin-tazobactam, or
            - Cefepime, or
            - Meropenem if high risk for ESBL

    AND

        - Antipseudomonal fluoroquinolone
            - Ciprofloxacin or levofloxacin

- *With risk factor for MRSA or patients with septic shock or respiratory failure requiring mechanical ventilation,* empiric regimens should include either vancomycin or linezolid
    - Linezolid is preferred if there is no bacteremia because:
        - Ability to inhibit bacterial toxin production
        - Better lung penetration
        - No need for monitoring AUC or MIC
    - Vancomycin is usually preferred if there is suspected or *known S. aureus* bacteremia

- *For patients with beta-lactam allergy*
    - Without risk factors for Pseudomonas or MDR pathogens
        - Respiratory fluoroquinolone plus aztreonam
    - With risk factors for Pseudomonas or MDR pathogens
        - Meropenem AND levofloxacin or ciprofloxacin IV, or
        - Aztreonam AND levofloxacin or ciprofloxacin IV plus aminoglycoside

As bacterial pathogens often coexist with viruses and there is no current diagnostic test accurate enough or fast enough to determine that CAP is due solely to a virus at the time of presentation ATS and IDSA guidelines recommend initially treat empirically for possible bacterial infection or coinfection.

INITIAL EMPIRIC ANTIBIOTIC SELECTION FOR HAP (*nvHAP or VAP)*

It is recommended a regimen that has activity against *Pseudomonas*, other gram-negative bacilli, and MSSA plus coverage for MRSA.

- Piperacillin-tazobactam, or
- Cefepime, or
- Meropenem if:
    - Prior history of ESBL, or
    - Consider for patients with VAP and risk factors for increased mortality
        - Septic shock at the time of VAP
        - ARDS preceding VAP
        - ≥5 days of hospitalization prior to the occurrence of VAP
        - Acute renal replacement therapy prior to VAP onset

    AND
- Vancomycin or linezolid
- On individual analysis a fluoroquinolone (levofloxacin or ciprofloxacin IV) or an aminoglycoside can be added for patients with increased mortality risk as stated above

Initial antibiotics for patients with special conditions

Chemical pneumonitis - Aspiration pneumonia

Prophylactic antibiotics for chemical pneumonitis

- N*ot indicated*
    - Patients with mild-to-moderate cases of chemical pneumonitis defined as PSI score ≤90
        - Withholding antibiotics is recommended regardless of the presence of lung infiltrates with clinical and radiographic reassessment in 48 hours
        - Antibiotics does not offer clinical benefit and may generate antibiotic selective pressures that results in the need for escalation of antibiotic
- *Indicated*
    - In moderate or severe cases of chemical pneumonitis defined as PSI score >90 and presence of lung infiltrates
    - In critically ill patients, even if there is no presence of lung infiltrates, with either:
        - Sepsis (organ failure attributed to the PNA)
        - Need for mechanical ventilatory support (IMV or NIV)

Routine treatment for anaerobic pathogens is not needed but indicated in those with:

- Poor dental health
- Necrotizing pneumonia
- Lung abscess or empyema
    - Piperacillin–Tazobactam, or
    - Meropenem, or
    - Combination of Metronidazole and Cefepime or Fluoroquinolones
    - Consider adding clindamycin

Confirmed penicillin or cephalosporin allergy

- Severe (IgE-mediated reactions, e.g., urticaria, angioedema, anaphylaxis), severe delayed reactions (e.g., Stevens-Johnson syndrome, toxic epidermal necrolysis)
    - Without risk factors for Pseudomonas or MDR pathogens
        - Fluoroquinolone, levofloxacin or ciprofloxacin oral or IV
    - With risk factors for Pseudomonas or MDR pathogens

        - Meropenem AND levofloxacin or ciprofloxacin oral or IV, or
        - Aztreonam AND levofloxacin or ciprofloxacin oral or IV
- Mild (non-IgE-mediated reactions, e.g., maculopapular rash)
    - A third or fourth-generation cephalosporin can safely be given with the doses stated above
    - Carbapenems have broader coverage but are also reasonable and safe alternatives for most patients
- Alternative for patient's intolerant to both beta-lactams and fluoroquinolones
    - Monotherapy with tigecycline
        - Limited use since it has been associated with increased mortality

Ceftazidime allergy

- Patients with a prior life-threatening or anaphylactic reaction (involving urticaria, bronchospasm, and/or hypotension) to ceftazidime should not be given aztreonam because of the possibility of cross-reactivity
    - Such patients can receive levofloxacin plus an aminoglycoside for antipseudomonal coverage

Prior documented resistance to carbapenems

- Will follow yearly IDSA guidelines and consult ID if not following the patient https://www.idsociety.org/practice-guideline/amr-guidance/

Presence of MDR pathogens that are only sensitive to colistin and/or aminoglycosides

- Will initiate inhaled antibiotic therapy in addition to the systemic therapy and consult ID if not following the patient

For patients with prior documented resistance to carbapenems (follow yearly IDSA guidelines https://www.idsociety.org/practice-guideline/amr-guidance/

- Empiric monotherapy with one of the following agents is recommended:
    - Ceftolozane-tazobactam 3 g IV every eight hours (preferred for *P. aeruginosa* infections)
    - Ceftazidime-avibactam 2.5 g IV every eight hours (preferred for *Enterobacterales* infections)
    - Meropenem- vaborbactam 4 g every eight hours (not active against carbapenem-resistant *P. aeruginosa* infections)
    - If the beta-lactam beta-lactamase agents listed above are not available and the suspicion is high, then the addition of one of the following agents along with a carbapenem is a reasonable alternative:
        - Respiratory fluoroquinolone
        - Aztreonam
        - Tobramycin
        - Colistin

Use of inhaled antibiotic therapy in addition to systemic therapy

- In the presence of MDR pathogens that are only sensitive to colistin and/or aminoglycosides

Prolonged QT interval

- Both the macrolides and the fluoroquinolones can cause a prolonged QT interval which can result in torsades de pointes
- Doxycycline is recommended for patients at high risk of QT interval prolongation. However, it should be noted that:
    - Doxycycline has been less well studied for the treatment of PNA than the macrolides and fluoroquinolones
    - The effect of azithromycin on prolonging the QT interval is controversial with literature showing no relevant unwanted effect
    - Doxycycline should be avoided during pregnancy

Newer antibiotics FDA approved (Omadacycline, Delafloxacin, Lefamulin)

- Because clinical experience with these agents is limited, their use is reserved for specific situations:
    - Alternate treatment options are not available or pose risk of adverse effects (eg, drug allergy or intolerance)
    - Patients who are unable to use a beta-lactam and wish to avoid the potential adverse effects associated with fluoroquinolones

Omadacycline (Nuzyra)

- Tetracycline derivative with activity against common atypical and typical CAP pathogens, MRSA, many gram-negative rods (but not *Pseudomonas* spp), and anaerobes

Delafloxacin (Baxdela)

- An extended-spectrum fluoroquinolone with activity against many respiratory pathogens including MRSA and *Pseudomonas* spp

Lefamulin (Xenleta)

- A systemic pleuromutilin with activity against MRSA, *S. pneumoniae*, and atypical CAP pathogens. However, apart from *H. influenza* and *M. catarrhalis*, its activity against certain gram-negative pathogens including Enterobacteriaceae (eg, *E. coli*, *Klebsiella* spp) and *Pseudomonas* spp is limited

Influenza treatment

A 5-day therapy with oseltamivir is recommended for all patients who test positive for the influenza virus and are admitted to the hospital

- Although there is no conclusive benefit to oseltamivir if started beyond 48 hours after symptom onset, still, any hospitalized patients with influenza must be treated with this agent regardless of the presentation time from the beginning of the illness

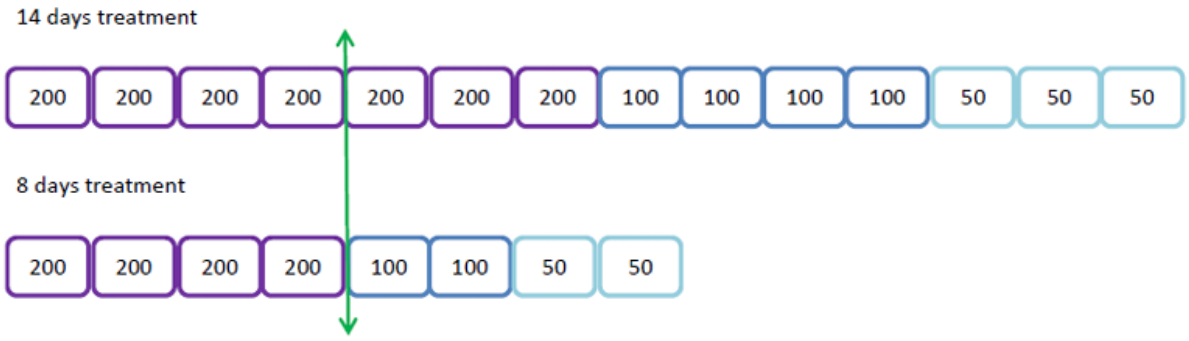
Use of adjunctive glucocorticoids

- Indicated in immunocompetent patients with severe PNA with any of the following conditions:
    - Need for invasive or non-invasive mechanical ventilation or HFNC
    - Severe hypoxemia: PaO2:FIO2 ratio <300 requiring FiO_2 ≥50%
- Avoid their use in patients with:

    - Certain infections
        - Influenza, fungi, tuberculosis, herpes, acute viral hepatitis
        - In immunocompromised patients weigh the risks and benefits on an individual basis
- Glucocorticoids are not withheld when they are indicated for other reasons, including septic shock, acute exacerbations of COPD, or COVID-19

Glucocorticoids regimen
Multiple dosing strategies are acceptable for severe CAP and left to clinician discretion. The most commonly recommended based on a RCT study is:

- Hydrocortisone IV continuous infusion 200 mg/d during the first 4 days
    - If clinical improvement on the fourth day
        - Taper hydrocortisone for a total treatment of 8 days
    - If no clinical improvement on the fourth day
        - Continue IV hydrocortisone infusion for 7 days and then initiate taper for a total treatment of 14 days



- In all cases, discontinue treatment at the time of discharge from the ICU

SUBSEQUENT MANAGEMENT

Duration of antibiotics
It is determined based on clinical improvement, microbiologic diagnosis, serial procalcitonin levels, underlying comorbidities, and the presence of complications.

Clinical response to therapy with appropriate antibiotic therapy is usually seen within 48 to 72 hours and most patients become clinically stable within three to four days of starting antibiotic treatment. Thus, the recommended duration for patients with good clinical response is usually five to seven days total.

- Although, data supporting the efficacy of shorter courses of therapy is growing, the ATS/IDSA guidelines still recommend that patients with CAP should generally be treated for a minimum of five days
    - Mild PNA generally require five days of therapy
    - Severe PNA or underlying chronic comorbidities generally require 7 to 10 days of therapy

- The duration of therapy may need to be extended beyond seven days in certain patients despite clinical stability and low procalcitonin levels
    - The initial therapy was not active against the subsequently identified pathogen
    - Extrapulmonary infection is identified (eg, meningitis or endocarditis)
    - Complications such as necrotizing PNA, parapneumonic effusions, empyema, or lung abscess
        - For lung abscess, until CT chest evidence of decreasing size or abscess resolution
    - PNA caused by *P. aeruginosa* or some unusual and less common pathogen (e.g., Burkholderia pseudomallei, fungus)
    - For MRSA PNA complicated by bacteremia, a minimum of two weeks of treatment is needed
        - Longer courses (e.g., ≥4 weeks) are needed for patients with metastatic complications of bacteremia and for immunocompromised patients
- Before stopping therapy, the patient should be:
    - Afebrile for 48 to 72 hours
    - No need for supplemental oxygen unless required for preexisting disease, and
    - Have no more than one clinical instability factor defined as:
        - HR >100 beats/minute
        - RR >24 breaths/minute, and
        - SBP ≤90 mmHg).
- Procalcitonin, although not required for the diagnosis of PNA, can be used to guide the decision to stop antibiotics.
    - It is recommended to obtain a level at the time of diagnosis and repeat levels in patients who are clinically stable and have been receiving antibiotics regardless of the duration with the intention to discontinue the antibiotics
- Radiographic response typically lags behind the clinical response
    - Infiltrates usually resolves within 4 to 6 weeks in younger population and 6 to 8 weeks in the elderly population
- Antimicrobial stewardship programs can help to shorten the duration of antibiotics and narrow the spectrum of antibiotics

Lack of response to antibiotics

Failure to respond to antibiotic treatment within 72 hours are considered non-responders and should prompt reconsideration of the diagnosis and empiric treatment regimen as well as assessment for complications.

Potential causes of non-resolving PNA include:

- Delayed clinical response particularly in those with multiple comorbidities, severe pneumonia, bacteremia, and infection with certain pathogens (eg, *S. pneumoniae*)
    - Treatment response may be slow
    - Eight or ten days of treatment may be needed before clinical improvement is evident
- Loculated infection
- Bronchial obstruction
- Pathogens that cause subacute/chronic CAP

    - Mycobacterium tuberculosis, nontuberculous mycobacteria, or less common bacteria (e.g., Nocardia spp., Actinomyces) can cause subacute or chronic PNA
- Incorrect initial diagnosis

Once a patient is characterized as having non-resolving PNA, a complete new physical examination, laboratory evaluation, imaging studies, and microbiologic workup will be necessary to define the etiology of non-resolving PNA.

- Initiation of workup for non-resolving PNA should not be automatically associated with a change in initial empiric antibiotic therapy.

Antibiotic de-escalation

Once a pathogen is established based upon reliable microbiologic methods, is recommended narrowing antibiotic therapy "de-escalation" to target the specific pathogen in order to avoid antibiotic overuse.

For patients who are clinically improving who do not have an identified pathogen, empiric treatment for MRSA*, Pseudomonas aeruginosa,* or multidrug-resistant (MDR) gram-negative bacilli can be discontinued if these organisms have not grown in culture from a high-quality sputum or bronchoalveolar lavage specimen within 48 to 72 hours.

Discontinuing empiric MRSA treatment for patients with negative nasal screening results is generally safe and can help avoid unnecessary antibiotic exposure.

IV to oral transition

- Patients should be switched from IV to oral therapy when they are:
    - Clinically improving and hemodynamically stable
    - Able to take oral medications and have a normally functioning gastrointestinal tract
- In patients who are treated with the combination of an IV beta-lactam and a macrolide
    - Replace the IV beta-lactam with high-dose amoxicillin-clavulanic to complete the course of therapy
        - If the patient have already received 1.5 g of azithromycin and do not have legionella PNA:
            - Amoxicillin-clavulanic alone, if not
            - Amoxicillin-clavulanic plus azithromycin or doxycycline
    - An alternative for patients without risk factors for drug resistant streptococcus pneumonia (DRSP) is to give a macrolide or doxycycline alone to complete the course of therapy.
- Patients who are treated initially with an IV respiratory fluoroquinolone or macrolide can be switched to the oral formulation of the same agent

Prevention

- Smoking cessation when applicable
- Yearly influenza vaccination for the general population
- COVID-19 vaccination
    - A 2023-24 mRNA vaccine regardless of previous vaccination

        - A single dose given at least 2 months after the most recent prior dose of COVID-19 vaccine for all non-immune-compromised patients
        - For patients with moderate to severe immune compromise, 3 or 4 vaccine doses are recommended
- Pneumococcal vaccination for at-risk populations
    - Either pneumococcal conjugate vaccine (PCV20) alone or PCV15 coupled with pneumococcal polysaccharide vaccine (PPSV23) one year later
    - PCV20 for patients who have never received any PCV or whose previous vaccination history is unknown
        - All patients ≥65 years old
        - Others with specific risk factors
            - Chronic heart, lung, and liver disease
            - Immunocompromising conditions including impaired splenic function
        - If PCV20 is used, a dose of PPSV23 is not indicated
        - If PCV15 is used, a dose of PPSV23 is needed one year later
    - For patients who already had vaccinations with prior PCV13 or PPSV23
        - Those who received only PCV13 can be followed by PPSV23 vaccination a year later
        - If the prior vaccine was only with PPSV23, then after a year, either PCV20 alone or PCV15 followed a year later with another PPSV23 can be given
- RSV vaccination for at-risk populations
    - All patients ≥75 years old
    - Ages 60-74 with specific risk factors as above and patients living in nursing homes
    - Currently is not an annual vaccine
    - Recommended in late summer and early fall
- Consider using a single dose of ceftriaxone 2 gr IV within the 12 h following intubation in patients with severe brain injury expected to require mechanical ventilation for at least 48 hours
    - Severe acute brain injury defined as ≤12 GCS after trauma, stroke, or subarachnoid hemorrhage.
- Will consider on a case-by-case analysis inhaled antibiotic therapy for critically ill patients undergoing invasive mechanical ventilation for at least 72 hours attempting to prevent VAP
    - Amikacin at a dose of 20 mg/Kg/IBW daily by nebulization, or
    - Tobramycin 300 mg by nebulization q12h

Discharge and follow-up

It is appropriate when the patient is:

- Clinically stable from the PNA
- Can take oral medication
    - In a case-by case situation patients can be discharge on IV antibiotics under ID direction
- Has no other active medical problems
- Has a safe environment for continued care

Early mobilization of patients in combination with the use of objective criteria for switching to an oral antibiotic regimen and for deciding on hospital discharge compared with usual care is associated with significantly shorter length of stay.

Patients who have been discharged from the hospital with PNA should have:

- A follow-up visit usually within one months and a later visit is often indicated to assess for resolution of PNA
    - Most patients with clinical resolution after treatment do not require a follow-up CXR unless the patient has risk for lung cancer
- Patient-centered discharge instructions including:
    - Medications – antibiotics regimen reconciliation
    - Encourage to keep head elevation out of the bed 30 to 45 degrees and good oral hygiene to prevent aspiration
    - Encourage patient mobility with ambulation
    - Collection of SDOH data and demographic information before discharge to better understand which patients are at higher risk for readmission

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