

Pneumonia in Immunocompetent Patients

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1 | QUESTION

A 66-year-old male presents to the emergency room with a history of non-productive cough for the past five days. The patient also reports subjective fever for the past five days, and shortness of breath for the past three days. He explains that initially his symptoms were mild and tolerable but have gotten progressively worse since yesterday, prompting him to seek medical attention today. He has known hypertension, for which he takes ramipril. His past medical history is otherwise unremarkable, and he has no recent travel history.

On examination, he is alert and oriented, slightly

ABSTRACT

Pneumonia is a leading cause of morbidity. Pneumonia is defined as a lung inflammation of infectious etiology. It can be subcategorized into Community Acquired Pneumonia, Hospital Acquired Pneumonia and Ventilator Acquired Pneumonia. Validated scores including the CRB-65, CURB-65 and PSI can guide decision-making between inpatient and outpatient management of pneumonia. While mild presentations can be managed through empiric treatment alone, more acute cases require identification of the infectious agent, initiation of empiric therapy, and subsequent de-escalation of treatment to the identified pathogen. This article aims to provide a framework for junior trainees to diagnose and manage pneumonia.

KEY WORDS

Community Acquired Pneumonia, Hospital Acquired Pneumonia, Ventilator Acquired Pneumonia, Empiric Treatment

tachycardic (108 bpm), tachypneic (29 breaths/min), with an O₂ saturation of 93% and a slightly elevated blood pressure (129 mmHg / 88 mmHg). He appears fatigued. Auscultation reveals wheezing. Oral temperature is 38.4°C. His chest radiograph shows evidence of a diffuse pulmonary infiltrate.

Assuming the most likely diagnosis, what would you do next?

- A. Admit him to the hospital and treat with levofloxacin
- B. Obtain sputum gram stain and culture
- C. Treat out-patient with azithromycin
- D. Treat out-patient with gentamicin
- E. Treat out-patient with levofloxacin

2 | ANSWER

C. The patient's symptoms are consistent with community acquired pneumonia (CAP), with the pulmonary infiltrates on chest x-ray further increasing the likelihood of this diagnosis. The patient's CRB-65 score is 1. Given that the point was attributed due to the age criterion, he does not need a hospital admission. For outpatient care of community acquired pneumonia, empiric treatment is often sufficient. Azithromycin is a good broad-spectrum antibiotic that will cover common CAP pathogens such as *Streptococcus pneumoniae*. Gentamicin only covers gram-negative bacteria and is therefore inadequate for CAP treatment. Fluoroquinolones such as levofloxacin are not recommended as first-line therapy for out-patient treatment of community acquired pneumonia. (1)

This article aims to provide an initial approach to pneumonia for junior trainees. The data presented follows guidelines from Quebec (Canada) and may not be applicable to other settings.

3 | INITIAL APPROACH

Pneumonia is defined as a lung inflammation caused by an infection of bacterial, viral or fungal etiology. (1) Host immunity, pathogen virulence and inoculum size interplay to modulate the risk of pneumonia. Routes of infection include micro-aspiration, macro-aspiration and hematogenous spread. (2) The most common symptoms are cough, sputum production, dyspnea, pleuritic chest pain, and deterioration in overall health. Common physical examination findings include tachypnea, tachycardia, fever, low oxygen saturation, dullness on percussion, diminished breath sounds, rales and/or rhonchi. (3)

3.1 | Diagnosis

The most commonly ordered test when investigating pneumonia is the chest radiograph (posteroanterior and lateral views). (4) Radiographic findings suggestive of pneumonia include lobar consolidates, pulmonary infil-

trates, and/or cavitations. (4) The presence of cavitations indicates tissue necrosis and the development of lung abscesses. In cases of upper lobe cavitations, clinicians must be cautious to rule out *Mycobacterium tuberculosis*. (5)

While chest radiograph (CXR) is the standard imaging test, it has some limitations including poor image quality. (6) Other diagnostic modalities include chest computerized tomography (CT) and lung ultrasound. (6) Although CT scan is more precise and may identify pneumonias that are not detected on CXR, it is associated with increased costs and exposure to radiation. (6) Lung ultrasound may be useful for bedridden and unstable patients for whom it may be difficult to obtain a CXR. (7)

Sputum cultures are warranted for all hospitalized patients with severe illness. (8) However, they have been shown to be effective in identifying the infectious etiology only about half of the time. (8) Rapid molecular tests such as PCR and LAMP have been shown to be promising techniques that would improve testing turnaround time and sensitivity. (8) Yet, some issues still remain in terms of the diagnostic capacity of these tests, and cost effectiveness studies are needed before they are put to use more widely. (8)

3.2 | Classification

Pneumonia can be subcategorized into three different diagnoses based on the context of acquisition: Community Acquired Pneumonia (CAP), Hospital Acquired Pneumonia (HAP), and Ventilator Acquired Pneumonia (VAP). (9) CAP is defined as the development of pneumonia symptoms outside of a hospital setting, or within the first 48 hours of hospitalization. If symptoms occur past the first 48 hours of hospitalization, the appropriate diagnosis is HAP. The third diagnosis, VAP, is defined by symptom development occurring 48 hours after intubation. (9)

3.3 | Community Acquired Pneumonia

CAP is a leading cause of hospitalization and morbidity. (1, 3) The most commonly isolated agent is *Streptococcus*

pneumoniae. Other pathogens include influenza A virus, *Mycoplasma pneumoniae* and *Chlamydophila pneumoniae*. (3) While respiratory viruses, typical bacteria and atypical bacteria are the most common identified etiologies, the pathogen is unidentifiable in up to 60% of CAP cases. (10) Suspicion of a causative agent should be based on the region, season, and patient risk factors. (11)

While the choice between inpatient and outpatient care is usually made by using clinical judgment, validated scores can help support this decision. (3, 12) Previous research reports that the CRB-65, CURB-65 and PSI scores are comparable in predicting mortality, (12) although some data suggests PSI has a stronger predictive power for 30-day mortality. (4) The CRB-65 does not require invasive testing and is simpler to apply. (4) The CURB-65 may be favorable if bloodwork is being ordered, and/or is easily accessible. (4, 11) Evidence suggests that PSI is more accurate for low-risk patients, although it requires more intricate testing including arterial blood gas. (11, 12) All things considered, the use of CRB-65 is favorable in primary care settings. (3, 4) Patients needing hospital admission can further be triaged between a general ward and an ICU admission, according to the criteria listed in IDSA/ATS guidelines. (1) See Table 1 for complementary information.

3.3.1 | Guidelines for Treatment

Once diagnosis and choice of hospital admission have been made, treatment may be initiated. Examples of first-line therapy for outpatient care include select macrolides, tetracyclines and -lactams. If no improvement is observed after 72 hours of therapy, respiratory fluoroquinolones are suggested as second-line options. (3) Since certain conditions can increase the risk of severe illness, antibiotic choice also depends on the presence of patient risk factors (Table 2).

For inpatient treatment, the recommended approach is based on the severity of the disease, with patients admitted to the ICU and those with risk factors receiving more intensive treatment with multiple drugs. (1, 4) It is recommended to order a sputum gram stain and culture, if possible, prior to initiating empiric therapy for CAP pa-

tients with severe presentations. (1) Further information on treatment choice, as well as the complete list of patient risk factors, is compiled in Table 2. See Figure 1 for management flow chart.

3.4 | Hospital Acquired Pneumonia

Admitted patients have an increased exposure to pathogens of the hospital environment. Direct contact with care providers, as well as intubation, tracheostomy, and other respiratory interventions can facilitate the spread of pathogens and increase risks of HAP. The most commonly isolated pathogens include gram-negative bacilli and *Staphylococcus aureus*, and clinicians should maintain a high suspicion for drug-resistant organisms. (13)

3.4.1 | Guidelines for Treatment

The main risk factor for a drug-resistant pathogen infection in HAP patients is antibiotic use in the past 90 days. (14) Clinicians must be cautious of the development of septic shock and need for ventilatory support secondary to pneumonia, as they have been associated with mortality. (13, 14)

In stable patients with HAP, physicians usually opt to order a sputum culture prior to initiating empiric therapy. (14) It is recommended that empiric treatment regimens be based on local or site-specific data regarding HAP-associated pathogens and corresponding antibiograms. All empiric treatment regimens for HAP should ideally cover pathogens such as *S. aureus*, and *P. aeruginosa* or other gram-negative bacilli. Aminoglycoside monotherapy should be avoided due to toxicity and poor lung penetration. (14)

3.5 | Ventilator Acquired Pneumonia

For VAP, important routes of infection include microaspiration and tracheal tube contamination. Bacteria form biofilms inside the tracheal tube and contaminate oropharyngeal secretions. As the tube is introduced into the airways, pathogens reach the lung parenchyma and

replicate. (15) While the main causative agent is *Pseudomonas aeruginosa*, other common pathogens include *Escherichia coli*, *Klebsiella pneumoniae*, and *Acinetobacter*, as well as gram-positive cocci such as *S. aureus*. (13)

3.5.1 | Guidelines for Treatment

Risk factors for a multidrug-resistant pathogen infections in VAP patients include: intravenous antibiotic use in the past 90 days, septic shock at the time of pneumonia onset, acute respiratory distress syndrome, 5 days of hospitalization, and acute renal replacement therapy prior to pneumonia onset. (14)

Similar to HAP, stable VAP patients should have bacterial cultures ordered prior to initiation of empiric treatment. The recommended lab investigation, in this case, is a semiquantitative culture of an endotracheal aspirate (ETA). This test was found to be the most sensitive when compared to other testing options for intubated patients (e.g. quantitative ETA, quantitative bronchoalveolar lavage, etc.). (14)

Empiric treatment regimens should be chosen according to local or site-specific data on VAP-associated pathogens and corresponding antibiograms. Empiric treatment regimens for VAP should cover pathogens such as *S. aureus*, and *P. aeruginosa* or other gram-negative bacilli. It is also recommended that the use of aminoglycosides and colistin be avoided. (14)

4 | BEYOND THE INITIAL APPROACH

4.1 | Considerations for Management

Whenever bacterial cultures are ordered prior to initiation of empiric therapy, treatment should be de-escalated to target the isolated pathogen. (1, 14) Since pneumonia is a presentation that can frequently lead to sepsis, blood cultures should be ordered to investigate bacteremia in severe presentations. (16)

Due to the association of pneumonia and pleural disease, clinicians must also be cautious of the development of effusion and empyema in patients not improv-

ing despite treatment. In these conditions, the patient may require invasive interventions including tube thoracostomy. (17)

For CAP, the course of antibiotics should last >5 days as a general rule. (1) For HAP and VAP, the recommended treatment duration is 7 days. (14) In all cases, treatment should only be discontinued once the patient reaches clinical stability. (1, 14)

The following evidence-based measures may be used to evaluate the patient's clinical stability: ability to eat, normal mentation, and vital signs including heart rate, respiratory rate, blood pressure, oxygen saturation, and temperature. (1) Procalcitonin levels may also be useful to determine if antibiotics should be discontinued, especially in patients with HAP or VAP. (14)

4.2 | Epidemic Pathogens

Additional tests may be recommended if the patient is suspected to have been exposed to epidemic pathogens. To identify influenza, a molecular assay test is recommended. In influenza positive patients, it is recommended to treat with oseltamivir or zanamivir. (11) For *Legionella*, a urinary antigen test will be useful. (14) If SARS-CoV2 is suspected, a nucleic acid amplification test (NAAT) should be ordered. (18)

In patients with viral infections, clinicians must remain cautious of the development of bacterial superinfections, as secondary infection with *S. aureus* or *S. pneumoniae* has been linked with significant morbidity. (19)

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5 | TABLES & FIGURES

CRB-65^a		PSI	
Score	Recommendation	Score	Recommendation
0	Very low risk; usually does not require hospitalization	<51	
1	Consider hospitalization; If 1 point is given due to the age criteria, use clinical judgment	51-70	Outpatient therapy should be considered, especially if score ≤70
2	Hospitalize	71-90	
3 or 4	Hospitalize	91-130	
CURB-65^b		>130	Patient should be hospitalized
Score	Recommendation	PSI point distribution and risk factors	
0	Low risk; consider home treatment	Points	Risk factor
1		Age (years): _____	Men
2	Short inpatient hospitalization or closely supervised outpatient treatment	Age (years) - 10: _____	Women
3	Severe pneumonia; hospitalize and consider admitting to intensive care	+10	Nursing home resident
4 or 5		+30	Neoplasm
CRB-65 and CURB-65 clinical factors (1 points each)		+20	Liver disease
Confusion		+10	Heart failure
Blood urea nitrogen >19 mg per dL		+10	Stroke
Respiratory rate ≥30 breaths per minute		+10	Renal failure
Systolic blood pressure <90 mm Hg or Diastolic blood pressure ≤60 mm Hg		+20	Altered mental status
Age ≥65 years		+20	Respiratory rate ≥30 breaths per minute
IDSA-ATS 2019^c		+20	Systolic blood pressure <90 mm Hg
Minor criteria		+15	Temperature <35°C or ≥40 °C
Respiratory rate ≥30 breaths per minute		+10	Pulse rate ≥125 beats per minute
Pa _{O₂} /Fi _{O₂} ratio ≤250		+30	Arterial pH <7.35
Multilobar infiltrates		+20	Blood urea nitrogen >30 mg per dL
Confusion/disorientation		+20	Sodium <130 mmol per L
Uremia (blood urea nitrogen level ≥20 mg/dL)		+10	Glucose ≥250 mg per dL
Leukopenia due to infection alone (white blood cell count <4,000 cells/µL)		+10	Hematocrit <30%
Hypothermia (core temperature <36 °C)		+10	Partial pressure of arterial oxygen <60 mm Hg
Hypotension requiring aggressive fluid resuscitation		+10	Pleural effusion
Major criteria			
Septic shock with need for vasopressors			
Respiratory failure requiring mechanical ventilation			

TABLE 1 CRB-65, CURB-65, PSI and IDSA-ATS summary

^aCRB-65 - Confusion, Respiratory rate, Blood pressure, 65 years of age and older.

^bCURB-65 - Confusion, Urea nitrogen, Respiratory rate, Blood pressure, 65 years of age and older.

^cIDSA-ATS 2019 guidelines - Patients should be considered for ICU admission if they satisfy either 1 major criteria, or 3 minor criteria.

Adapted from:

Institut national d'excellence en santé et en services sociaux. Pneumonie acquise en communauté chez l'adulte [Internet]. 2017. Available from: https://www.inesss.qc.ca/fileadmin/doc/CDM/UsageOptimal/Guides-seriel/INESSS_Annexes_Rapport_GOU_PAC.pdf.

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COMMUNITY-ACQUIRED PNEUMONIA			Antibiotic combinations		
OUTPATIENT TREATMENT	First-line	Second-line	A	Macrolide (Clarithromycin or Azithromycin), Tetracycline (Doxycycline), Beta-lactam (High-Dose Amoxicillin)	
Risk Factors^a: Absent	Choose one from A	Choose a different one from A OR Dual-therapy (one from each list) from B	B	High-dose amoxicillin, Amoxicillin-clavulanate	Clarithromycin, Azithromycin, Doxycycline
Risk Factors^a: Present	Dual-therapy (one from each list) from B	Choose one from C	C	Levofloxacin, Moxifloxacin	
INPATIENT TREATMENT	General ward admission	ICU admission	D	Ampicillin-Sulbactam, Cefotaxime, Ceftriaxone OR Ceftaroline	
Baseline coverage (Risk Factors^b: Absent)	Choose one each from D & E OR one from C	Choose one from D AND one from either C or E	E	Clarithromycin, Azithromycin	
Risk Factors^b: Present for MRSA	Baseline coverage above + Choose one from F		F	Vancomycin, Linezolid	
Risk Factors^b: Present for <i>P. Aeruginosa</i>	Baseline coverage above + Choose two from G		G	Piperacillin-Tazobactam, Cefepime, Ceftazidime, Imipenem, Meropenem, Aztreonam	

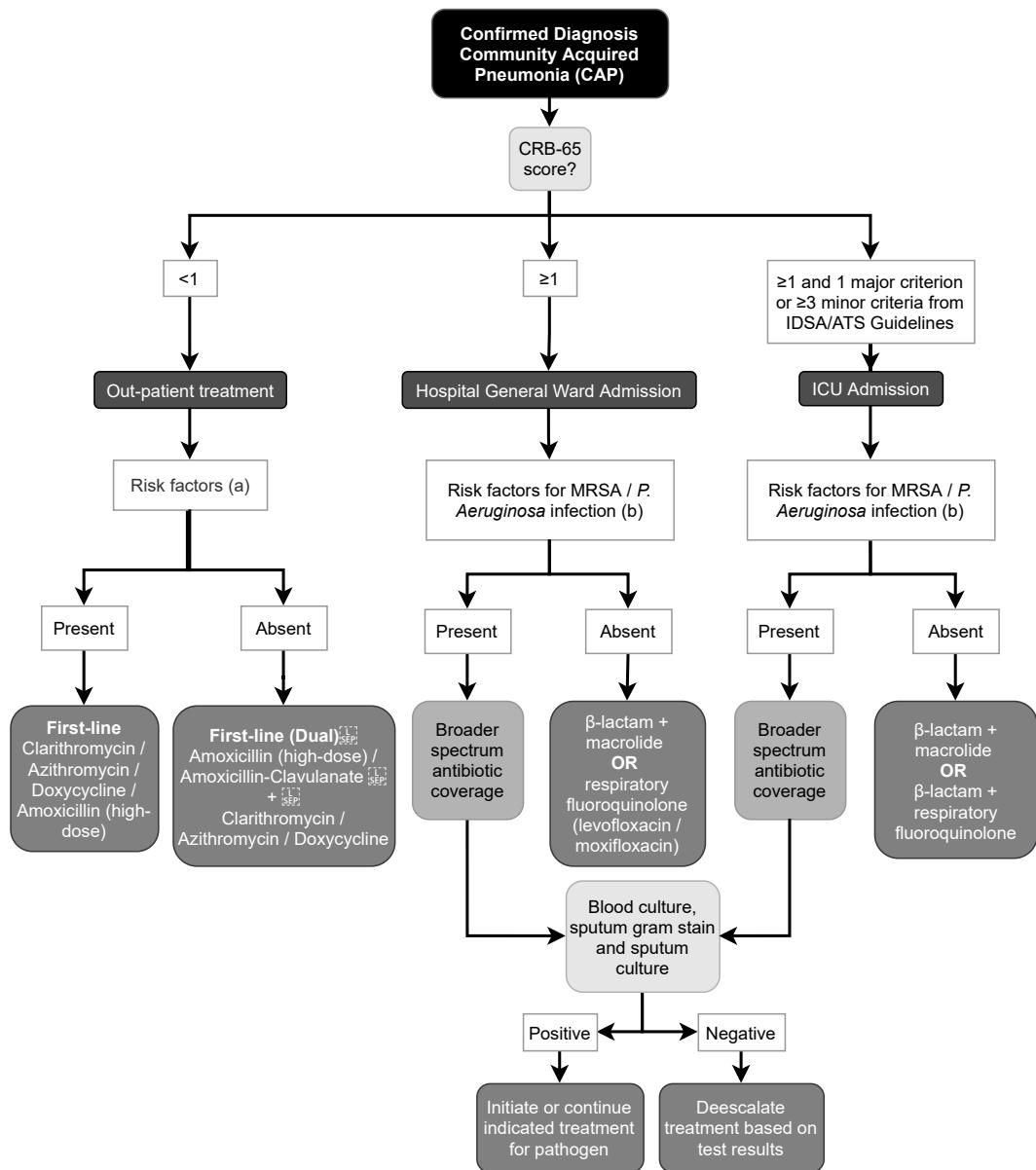
TABLE 2 Antibiotic therapy for community acquired pneumonia, according to inpatient or outpatient care and presence of risk factors.

^aOutpatient: Risk factors to consider include smoking; antibiotic use in the past 90 days; chronic heart, lung, kidney, or liver disease; diabetes mellitus; alcohol dependence; immunosuppression.

^bInpatient: Specific risk factors for MRSA or *P. Aeruginosa* include: Previous infection with the pathogen, recent hospitalization, recent use of parenteral antibiotics, site-specific risk factors for either pathogen.

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FLOWCHART 1 Flow chart for management of community acquired pneumonia

^aOutpatient: Risk factors to consider include smoking; antibiotic use in the past 90 days; chronic heart, lung, kidney, or liver disease; diabetes mellitus; alcohol dependence; immunosuppression.

^bInpatient: Specific risk factors for MRSA or *P. aeruginosa* include (10):

- Previous infection with the pathogen
- Recent hospitalization
- Recent use of parenteral antibiotics
- Site-specific risk factors for either pathogen

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