Review

TRANSLATIONAL&PRACTICAL MEDICINE

DOI: 10.51271/JTPM-0054
J Transl Pract Med. 2023;2(3):126-134

Pneumonies

Esma Sevil Akkurt[1], Mustafa Bayraktar[2]

[1]Department of Chest Disease, University of Health Sciences Ankara Atatürk Sanatorium Training and Research Hospital, Ankara, Turkey
[2]Department of Internal Medicine, Kırıkkale Public Hospital, Kırıkkale, Turkey

Cite this article as: Akkurt ES, Bayraktar M. Pneumonies. *J Transl Pract Med.* 2023;2(3):126-134.

Received: 28/11/2023 • **Accepted**: 29/12/2023 • **Published**: 31/12/2023

ABSTARCT

Pneumonia is an inflammation of the alveolar space distal to the terminal bronchiole in the lung parenchyma. The inflammation seen in pneumonia is mostly caused by microorganisms such as viruses, bacteria, and fungi, but can also be caused by non-infectious causes (toxic substance inhalation, radiation damage, hypersensitivity reaction-pneumonitis, autoimmunity). Pneumonia can be observed in three forms: community-acquired pneumonia (CAP), hospital-acquired pneumonia (HAP), and ventilator-associated pneumonia (VAP). Patients with pneumonia usually present with cough, fever, sputum, chest pain, dyspnea, and hemoptysis. In addition, patients may have nonspecific symptoms. CAPs are caused by typical (*Streptococcus pneumoniae*) and atypical (*Chlamydia pneumoniae, Mycoplasma pneumoniae,* and *Legonella pneumoniae*) agents. On presentation, fever, pulse rate, respiratory rate, oxygen saturation, blood pressure, and auscultation should be performed. Typical chest radiographic findings in the diagnosis of CAP include lobar consolidations, interstitial infiltrates, and/or cavitations. Acute-phase reactants may be elevated in response to infection and inflammation in pneumonia. The first decision to be made in cases of pneumonia is the determination of the need for hospitalization and the choice of antibiotherapy. If possible, cultures should be taken before antibiotics are started on the patient for whom hospitalization is planned. After 72 hours, in patients with no symptom improvement, the reason for treatment non-response should be evaluated, and antibiotherapy should be changed if necessary.

Keywords: Antibiotherapy, community-acquired pneumonia Pneumonia, hospital-acquired pneumonia

INTRODUCTION

Pneumonia is an inflammation of the alveolar space distal to the terminal bronchiole in the lung parenchyma. The inflammation seen in pneumonia is mostly caused by microorganisms such as viruses, bacteria, and fungi, but can also be caused by non-infectious causes (toxic substance inhalation, radiation damage, hypersensitivity reaction-pneumonitis, autoimmunity). Leukocytes and fibrinous exudate getting into the alveolar space can make it hard for the lungs to work, which could mean they need invasive mechanical ventilation and intensive care.[1]

Pneumonia can be observed in three forms: community-acquired pneumonia (CAP), hospital-acquired pneumonia (HAP), and ventilator-associated pneumonia (VAP).[2,3]

Community Acquired Pneumonia

Pneumonia caused by community-acquired pathogens in people without a diagnosis of immunodeficiency is considered community-acquired pneumonia.

Hospital-Acquired Pneumonia

It is defined as pneumonia that develops within 48 hours before hospitalization and within the first 48 hours after discharge of the patient who was not in the picture of pneumonia.

Ventilator Associated Pneumonia it is defined as pneumonia that develops 48 hours after intubation in a patient under invasive mechanical ventilation support without pneumonia before intubation.

COMMUNITY-ACQUIRED PNEUMONIA

Pneumonia caused by community-acquired pathogens in individuals without a diagnosis of immunodeficiency is defined as community-acquired pneumonia (CAP).[4] Community-acquired pneumonia (CAP) is responsible for a significant portion of mortality and morbidity worldwide.[5] Newly developing infiltrations on chest radiography, together with appropriate clinical and laboratory findings, are the gold standard for diagnosis.[6] The clinic is characterized by the acute onset of fever,

Corresponding Author: Esma Sevil Akkurt, esma.sevil@hotmail.com

cough (with or without sputum), and dyspnea. In some cases, pleuritic chest pain may also accompany. Less common symptoms include gastrointestinal complaints (nausea, vomiting, diarrhea, and abdominal pain) and loss of appetite. In older patients, fever may be absent or mental status changes may be the only presenting symptom.[7] Identification of the responsible microorganism is important for treatment, but since it is often not possible to identify the causative agent, it is necessary to start empirical treatment as soon as possible by correctly estimating the possible agents. For this reason, it is important to evaluate the patient's clinical picture, lung radiographic findings, the patient's risk factors, and, if possible, the results of sputum gram staining. Table 1 shows the risk factors associated with specific pathogens in CAP.[8]

Table 1. Risk factors associated with specific pathogens in community-acquired pneumonia

Alcoholism	*Streptococcus pneumoniae,* Oral anaerobes, *Klebsiella pneumoniae, Acinetobacter* species, *Mycobacterium tuberculosis*
COPD and/or smoking	*Haemophilus influenzae, Pseudomonas aeruginosa, Legionella* species, *S. pneumoniae, Moraxella catarrhalis, Chlamydia pneumoniae*
Aspiration	Gram-negative enteric oral anaerobes pathogens, oral anaerobes
Lung abscess	MRSA, oral anaerobes, endemic fungal pneumonia, *M. tuberculosis*, atypical mycobacteria
Exposure to bat or bird droppings	*Histoplasma capsulatum*
Feeding birds	*Chlamydia psittaci*
Feeding rabbits	*Francisella tularensis*
Keeping farm animals or cats	*Coxiella burnetti* (Q fever)
HIV infection (early)	*S. pneumoniae, H. influenzae, M. tuberculosis*
HIV infection (late)	Pathogens listed for early infection *Pneumocystis jirovecii, Cryptococcus, Histoplasma, Aspergillus,* Atypical mycobacteria (especially *Mycobacterium kansasii*), *P. aeruginosa, H. Influenzae*
Hotel or air-conditioned accommodation	Legionella species
Structural lung disease (e.g. bronchiectasis)	*P. aeruginosa, Burkholderia cepacia, S. aureus*
Injection drug use	*S. aureus,* Anaerobes, *M. tuberculosis, S. pneumoniae*
Endobronchial obstruction	Anaerobes, *S. pneumoniae, H. influenzae, S. aureus*

Risk Factors

Advanced age, the presence of comorbid diseases, malnutrition, immunosuppressive conditions, the presence of cognitive disease, and smoking all increase the risk of developing pneumonia. The most common comorbidities are COPD, hypertension, cerebrovascular diseases, heart failure, and malignancies.[9]

Clinic

Patients with pneumonia usually present with cough, fever, sputum, chest pain, dyspnea, and hemoptysis. In addition, patients may have nonspecific symptoms (nausea and vomiting, sore throat, myalgia, headache, etc.). CAPs are caused by typical (*Streptococcus pneumoniae*) and atypical (*Chlamydia pneumoniae, Mycoplasma pneumoniae,* and *Legonella pneumoniae*) agents. These agents have different clinical manifestations. In typical pneumonia, acute onset, fever, cough, chest pain (pleuritic), lobar infiltrations on chest radiography, and leukocytosis-neutrophilia in the complete blood count are present. In atypical pneumonias, subsegmental infiltrations, scattered patchy infiltrations, reticular opacities, and a normal leukocyte value in the complete blood count are observed on chest radiography, with nonspecific findings including subacute onset, subfebrile fever, myalgia, and headache.[4,6,9]

Physical Examination

On presentation, fever, pulse rate, respiratory rate, oxygen saturation, blood pressure, and auscultation should be performed. Pneumonia may present with tachycardia, tachypnea, and hypoxemia on physical examination.

Auscultation findings vary according to stage and extent.

*Thin rales (crepitant rales) at the end of inspiration in the exudation phase,

*Bronchial respiration during the consolidation phase (tuber sufl),

*In the resolution phase, fine rales are heard again.[10]

Radiology

Two-way chest radiography should be performed in patients with a suspected diagnosis of pneumonia, unless there is an obstacle. Posteroanterior and lateral chest radiographs are sufficient for diagnosis in most patients with suspected CAP. Imaging is a necessity for hospitalized patients.[7] Typical chest radiographic findings in the diagnosis of CAP include lobar consolidations, interstitial infiltrates, and/or cavitations. Findings on x-rays can help doctors figure out what caused pneumonia (for example, lobar consolidations can mean an infection with common bacterial pathogens), but they can't always tell the difference between them.[11]

Chest radiography is guiding both the diagnosis and the detection of a condition mimicking pneumonia. It is not possible to make a definite etiologic diagnosis with radiologic appearance, but it may be useful in the differential diagnosis of certain diseases such as tuberculosis and cancer.[12] It is also helpful in the detection of complications of pneumonia (e.g., parapneumonic effusion, empyema, abscess) and in the evaluation of alternative or concurrent diagnoses (e.g., heart failure, malignancy).[7] Lung imaging is also useful to determine the severity of pneumonia (such as multilobar involvement). Lobar (Figure 1), segmental, bronchopneumonic, and interstitial involvement (Figure 2) can be seen on chest radiography. When chest radiography is performed within the first 4 hours in patients with suspected pneumonia, mortality is significantly reduced due to the acceleration of diagnosis and the initiation of effective treatment.[4]

After the diagnosis of pneumonia and the initiation of treatment, radiologic control varies according to the clinical status of the patient and the presence of complications. While it is sufficient to see the patient once the treatment is completed in pneumonias with response, in cases of delayed resolution (no radiologic improvement after 4-6 weeks despite clinical response), recurrent pneumonias (at least two pneumonias in a year or at least three pneumonias in a lifetime), lung radiography follow-up and thoracic computed tomography evaluation may be required in terms of complications.[12]

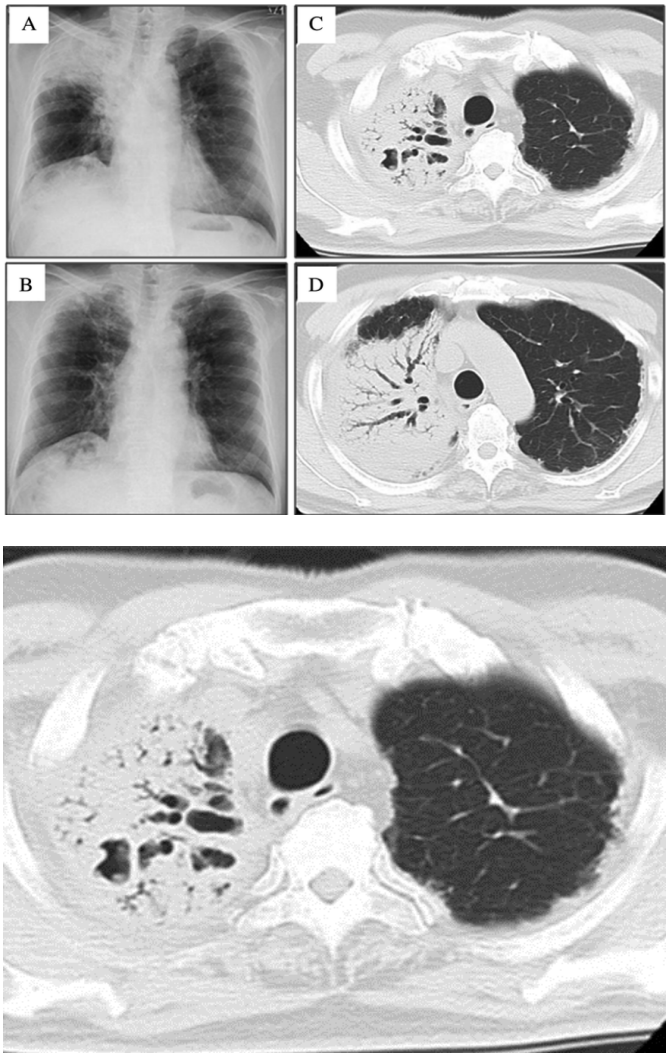

Figure 1. Lobar pneumonia, chest radiography, and lung computed tomography findings (air bronchograms)

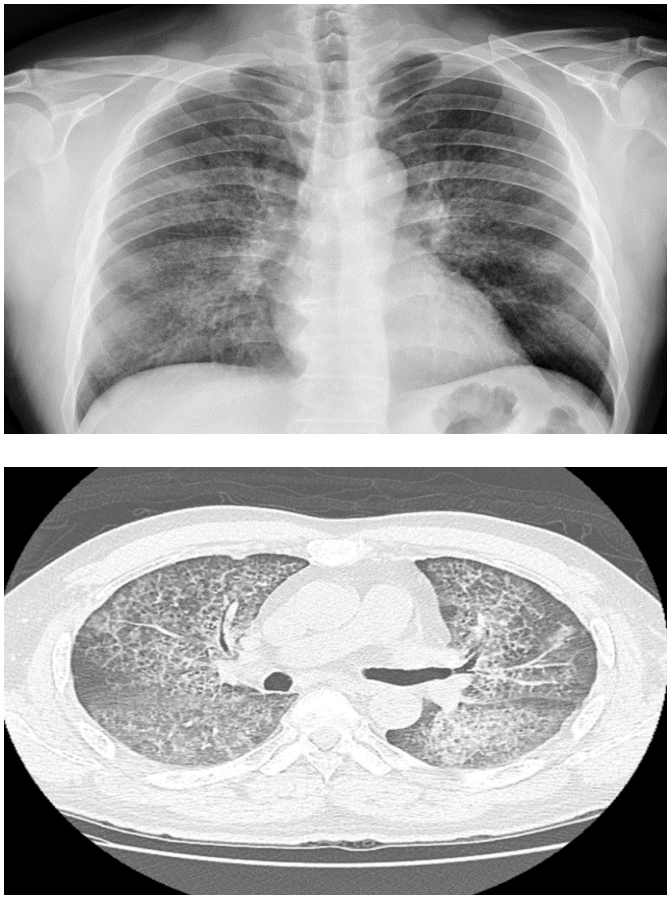

Figure 2. Chest radiography and lung computed tomography findings in interstitial pneumonia

It should be kept in mind that chest radiography may appear normal in the first 24 hours of pneumonia, in elderly patients, in the presence of neutropenia, in dehydration, and in *Pneumocystis jiroveci* pneumonia.[13]

High-resolution computed tomography (HRCT) is more sensitive than chest radiography in the detection of pneumonia.[5] It may help differentiate pneumonia complications and some pneumonia agents (e.g., invasive fungal infections, pneumocyst pneumonia, bacterial pathogens), especially in immunocompromised patients.[14] Thoracic CT imaging may be performed in patients with no improvement or deterioration in the clinic or in patients in whom other accompanying pathologies, such as tumors, are suspected.

Microbiological Investigations

Routine microbiologic examinations are not recommended for patients scheduled for outpatient follow-up. Microbiological investigations are instructive in patients who are scheduled for hospitalization and in patients with a history of colonization due to lung parenchymal injury. In patients requiring hospitalization, microbiologic investigations should be performed before antibiotherapy is started, if possible. Sputum culture samples should be evaluated together with gram staining, considering the possibility of colonization. It is recommended that blood cultures be sent separately from both arms during the febrile period.[4,10]

Microscopy of sputum and lower respiratory tract samples, blood, and sputum cultures are guiding the choice of treatment. However, it should be known that culture results are obtained in 24-48 hours under the best conditions. For this reason, it is not recommended to wait for culture results, even for patients who are sent for culture. Empirical antibiotherapy for the possible agent should be initiated at the time of diagnosis according to the clinical characteristics of the patient.[12]

In each patient, a microbiologic examination should be decided by evaluating the time and cost of proving the pathologic agent.

a. Evaluation of sputum by gram staining method; in microscopy of a quality sputum sample, the number of squamous epithelial cells seen with a small magnification objective (10x) should be less than 10, and the number of polymorphonuclear leukocytes (PNL) should be above 25. It is an important diagnostic method for the detection of the causative microorganism and the determination of antibiotic susceptibility. The sample must be obtained before antibiotic treatment is started. Sputum culture should be evaluated with gram staining.

b. Blood culture and PCR tests; rapid nasal PCR or culture tests are used in patients with risk factors for methicillin-resistant Staphylococcus aureus (MRSA).

c. In every hospitalized patient, two sets of blood cultures (one aerobic blood culture bottle + one anaerobic blood culture bottle) should be taken before antibiotic treatment is started and, if possible, during the febrile period.

d. In patients with parapneumonic pleurisy, pleural fluid cell count, biochemical examination of the fluid (pH, LDH, glucose, ADA, etc.), gram staining examination and cultures should be performed.

e. Molecular tests; viruses and bacteria are common infectious agents. Some of the bacteria causing respiratory tract infections cannot be grown in culture, and special media are needed for their growth (e.g., *Chlamydia pneumoniae, Legionella pneumophila, Mycoplasma pneumoniae*). Since viruses cannot be diagnosed by bacteriological culture, nucleic acid tests for viruses have been developed. Urine antigen tests for *Streptococcus pneumoniae*, polymerase chain reaction [PCR] for *Legionella* spp., or alternatively, urine antigen tests, and appropriate tests for COVID-19 can be performed.

Laboratory

Acute-phase reactants may be elevated in response to infection and inflammation in pneumonia. Acute-phase reactants and biomarkers may guide the differentiation between infectious and noninfectious diseases and the prognosis. A complete blood count, serum electrolytes, and renal and liver function values have a limited contribution to the diagnosis. However, they should be considered in prognosis, hospitalization evaluation, antibiotherapy selection, and dose adjustment. Blood gas measurement is recommended in the presence of COPD, hypotension, dyspnea, tachypnea, and confusion.[15]

Routine blood tests: Hemograms and biochemical tests are usually used to help confirm the diagnosis of CAP and determine the need for hospitalization.

a. Leukocytosis: Leukocytosis and left shift are most common in CAP. Leukopenia (<4000 cells per mm^2) is less common but usually means a worse prognosis. Similarly, thrombocytopenia (platelet count <100.000 cells per mm^2) is an uncommon finding, but like leukopenia, thrombocytopenia is associated with a poor prognosis.

b. Acute elevation of creatinine and BUN also implies a poor prognosis and often indicates the need for hospitalization. Abnormal liver function tests may be elevated in sepsis, requiring intensive care.

c. Serum biomarkers C-reactive protein (CRP) and procalcitonin support clinical and radiographic evaluation in the diagnosis of pneumonia.

Management of CAP Patients

The first decision to be made in cases of pneumonia is the determination of the need for hospitalization and the choice of antibiotherapy. Hospitalization is mainly related to the predicted prognosis. There are various scoring systems for determining the prognosis. Among these, CURB-65 and PSI (pneumonia severity index) are most commonly used (Table 2, Table 3, Table 4,, Table 5).[16,17]

Table 2. CURB-65 scoring
Confusion
Urea >42.8 (BUN >20 mg/dl or 7 mmol/l)
Respiratory rate >30/min
Blood pressure systolic <90 or diastolic <60 mmhg
Age >65
Each of the above criteria is a score → 0-1 low risk, 2 medium risk, 3-5 high risk

Table 3. Mortality risk level according to the CURB-65 score and assessment for hospitalization

Score	30-day mortality risk	Treatment location
0	<1%	Outpatient
1	3%	Outpatient but individual assessment required*
2	13%	Hospital
3	17%	Hospital
4	42%	Hospital - evaluation in terms of intensive care unit hospitalization required
5	57%	Assessment for hospital-intensive care unit hospitalization required

*Patients with inadequate home care support, patients with doubts about regular use of medications and adequate nutrition, and patients with criteria other than age in CURB-65 scoring may be hospitalized.

Table 4. Pneumonia associated severity score (PSI)

PSI score components	
Factor	**Score**
Patient age	
Male	Age
Female	Age-10
Long-term care facility resident	+10
Accompanying disease	
Neoplastic disease	+30
Liver Disease	+20
Congestive Heart Failure	+10
Cerebrovascular disease	+10
Chronic kidney disease	+10
Symptoms at diagnosis	
Acute psychosis	+20
Breathing rate >30/min	+20
Systolic pressure <90mmHg	+15
Body temperature <35 or >40	+15
Heart rate >125/min	+10
Laboratory measurements	
Arterial blood pH<7.35	+30
BUN >30mg/dl	+20
Serum sodium <130 mEq/L	+20
Serum glucose >250 mg/dl	+10
Hb<9gm/dl (hematocrit <%30)	+10
Atmospheric arterial blood gas (PaO_2)<60 mmHg	+10
SaO_2<90%	+10

Patients who do not require hospitalization, according to PSI and CURB-65 (Group 1), are followed and treated as outpatients. The group requiring hospitalization is evaluated according to the suitability of ward follow-up or intensive care unit follow-up (Group 2). Patients in Group 3 must be followed up in centers with intensive care. The approach according to disease severity is shown in Table 6.

Table 5. Assessment of mortality risk and hospitalization according to the PSI score

Risk Group	PSI score	30-day mortality risk	Treatment location
I-II	<70	<1%	Outpatient
III	71-90	1-3%	Outpatient, but individual assessment is required
IV	91-130	8-12%	Hospital
V	>130	27-31%	Assessment for hospital-intensive care unit hospitalization required

Table 6. Approach according to disease severity

	Disease severity	Treatment location	Microbial research
Mild	PSI: I or II or CURB-65:0	Outpatient treatment	COVID-19 testing during the pandemic Influenza testing (when incidence is high) Otherwise, the search for the causative pathogen is usually not necessary.
Middle	PSI: III or IV or CURB-65: 1-2	Hospitalization (ward)	Blood cultures Sputum Gram stain and culture urine streptococcal antigen *Legionella* test Respiratory viral panel during respiratory virus season COVID-19 test HIV screening
Severe	PSI: V or CURB-65>3	Hospitalization in the intensive care unit	Blood cultures sputum Gram stain and culture urine streptococcal antigen test *Legionella* test respiratory viral panel Bronchoscopy specimens for Gram stain, fungal stain, aerobic fungal culture, and molecular tests (when available) COVID-19 test for HIV screening

The criteria for the need for intensive care are given in Table 7.

Treatment

Early diagnosis and treatment of CAP are important in reducing mortality and morbidity. The choice of empirical antibiotherapy is determined according to patient groups. In pneumonia, patients are divided into three groups.

Group 1: Patients with a CURB65 score below 2 or PSI I-III who are followed as outpatients. Group 1 is divided into two groups. Patients without chronic disease are evaluated as Group la, and those with chronic disease are evaluated as Group lb.[17]

Table 7. Criteria for hospitalization in the intensive care unit
Major
The need for invasive mechanical ventilation
Septic shock requiring vasopressors
Minor
Respiratory rate >30/min
Pao2/fio2 <250
Multilobular infiltrates on chest radiograph
Uremia (BUN >20mg/dl)
Leukopenia (leukocytes <4000/mm³) Thrombocytopenia (platelets <100000/mm³)
Hypothermia (<36c)
Hypotension requiring intensive fluid loading
In the presence of one of the major risk factors or at least three of the minor risk factors, intensive care unit monitoring is recommended.

Possible pneumonia agents in group la are *Streptococcus pneumoniae, Mycoplasma pneumoniae,* and *Chlamydophila pneumoniae*. While penicillin/amoxicillin treatment is sufficient in the clinical picture of typical pneumonia, if atypical pneumonia is considered, it is recommended to add a macrolide group to penicillin/ampicillin.[9,17,18]

In group 1b, possible agents increase due to the presence of chronic disease. *Haemophilus influenzae* and enteric Gram-negative bacilli are added to the agents in group 1a. In treatment, 2nd-3rd generation oral cephalosporin alone or combined with macrolide or doxycycline, amoxicillin clavulanic acid alone or combined with macrolide or doxycycline, and monotherapy with respiratory quinolone alone can be applied.[9,17,18] (Table 8)

It should be emphasized that patients with a treatment plan should be readmitted if there is no clinical improvement (decrease in fever, regression in symptoms) after 72 hours.

Group 2 is a group of patients with a CURB-65 score of 2 and above or PSI IV-V who do not meet intensive care criteria. Requires ward follow-up. Group 3 includes patients with a CURB-65 score of 2 and above or between PSI IV-V who meet intensive care criteria.[18,19]

Risk factors for resistant infection should be taken into consideration when choosing empiric antibiotherapy in groups 2 and 3. Isolation of resistant bacteria in the respiratory tract in the last 6 months, hospitalization in the last 3 months, and history of antibiotic use in the last 3 months are risk factors for resistant infection.[19]

The antibiotherapy selection is similar for both groups. Patients without resistance risk factors are primarily recommended betalactam-betalactamase inhibitors without anti-Pseudomonas activity or macrolide

Table 8. Group 1 treatment algorithm		
	Possible factors	**Recommended antibiotics**
Group 1a (without chronic diseases)	-*Streptococcus pneumonia* -*Mycoplasma pneumonia** -*Chylamadolphylia pneumonia** - viruses	-amoxicillin -amoxicillin + macrolide / doxycycline **
Group1b (those with chronic diseases)	Group 1a bacteria *Haemophilus influenzae* Enteric gram-negative bacilli	-2nd-3rd generation oral cephalosporin -2nd-3rd generation oral cephalosporin + macrolide / doxycycline ** -amoxicillin clavulanic acid -amoxicillin clavulanic acid + macrolide / doxycycline ** - monotherapy with respiratory quinolone ***
*Some bacteria can cause pneumonia alone or together with another bacteria (mixed infection) **Decision should be made by showing a syndromic approach. *** In patients considering a combination of beta-lactam + macrolide/doxycycline, if there is a history of gastrointestinal problems, drug allergies, or a history of beta-lactam use in the last 3 months, it is more appropriate to use a respiratory fluoroquinolone alone instead of this combination. Quinolones should not be used in patients with clinical or radiographic evidence of tuberculosis.		

combinations with 3rd generation cephalosporins (cefotaxime and ceftrisxone) without anti-Pseudomonas activity, while macrolide combination therapy with broad-spectrum anti-*Pseudomonas* active antibiotics is recommended for patients with risk factors. The only difference between the two groups is that while respiratory quinolone monotherapy is appropriate in patients hospitalized in the ward, one of the options of beta-lactam+macrolide or beta-lactam+respiratory quinolone is recommended in patients hospitalized in intensive care due to the lack of sufficient data on the efficacy of quinolone monotherapy.[17,20](Table 9)

Priority parenteral antibiotherapy is recommended in cases of pneumonia requiring hospitalization. In order to reduce the cost, complications, and hospitalization of parenteral treatment, a transition to oral treatment is recommended for patients who respond to treatment (Table 10). This requires a fever-free period of at least 24 hours, resolution of tachycardia, tachypnea, hypotension, and hypoxemia, regression of leukocytosis and CRP levels, and no problems with oral intake and gastrointestinal absorption. Antibiotics can be discontinued after the fever subsides and the patient is clinically stable, provided that the total duration of treatment is not shorter than 5 days (7 days in resistant infections).[20]

Table 9. Group 2 and Group 3 treatment algorithm

Patients without risk factors for the resistant agent	Possible factors	Recommended antibiotics
Patients without risk factors for the resistant agent	-*Streptococcus pneumonia* -*Legionella pneumophilia* -*Haemophilus influenza* -enteric gram-negative bacilli -*Staphylococcus aureus* -*Mycoplasma pneumonia* -viruses	*3rd generation anti-pseudomonas non-cephalosporin (3ksef)+macrolides *betalactam + betalactamase inhibitor (bl+bli)+ macrolide *respiratory fluoroquinolone (patients hospitalized in the ward) 3k sef or bl + bli+ respiratory fluoroquinolone (patients hospitalized in the ICU)
Patients with risk factors for a resistant agent	-Factors in patients without risk factors -pseudomonas aeruginosa -Enteric gram-negative bacilli producing extended spectrum beta lactamase (gsbl)	*anti-*Pseudomonas* beta lactam*+ ciprofloxacin Anti-pseudomonas beta lactam*+ aminoglycoside +macrolide

The presence of these bacteria isolated from respiratory samples within the last year, antibiotic use in the last 3 months, and hospitalization history in the last 3 months
In hospitalized patients, risk factors for resistant infection are common, and there is no significant difference in antibiotic choices, regardless of the need for ICU admission (severity of pneumonia). However, in the absence of data on the efficacy of respiratory quinolone monotherapy in severe pneumonia requiring intensive care, combination therapy is recommended.
*In patients in whom broad-spectrum antibiotic treatment has been initiated, bacteriologic examination results should be monitored, and in cases where a bacterium is isolated, treatment should be rearranged according to the antibiogram result, and de-escalation should be performed if possible (the spectrum should be narrowed).
*3rd generation cephalosporin (ceftazidime), 4th generation cephalosporin (cefepime), carbapenems(imipenem, meropenem), beta-lactamase inhibitor anti-pseudomonas drugs (piperacillin + tazobactam, cefoperazone + sulbactam)
* Patients on ciprofloxacin do not need to add a macrolide.

Table 10. Antibiotics used in sequential treatment

IV/ With the same antibiotic orally	IV/ With oral different antibiotics
Cefuroxime / cefuroxime axetil Amoxicillin-clavulanic acid Clarithromycin Ciprofloxacin Levofloxacin Moxifloxacin Clindamycin Metronidazole	Cefotaxime/cefuroxime axetil . Cefotaxime/cefixime Ceftazidime/ciprofloxacin - Ceftriaxone/cefixime Ampicillin-sulbactam/ Amoxicillin-clavulanic acid

Treatment non-response is the absence of improvement in fever and other symptoms 72 hours after the initiation of antibiotherapy. Treatment non-response, patient compliance, appropriateness of antibiotherapy, development of complications such as empyema or abscess, and additional diseases or conditions that may make recovery difficult should be reviewed.[18]

HOSPITAL-ACQUIRED PNEUMONIA

Pneumonia that develops 48 hours after hospitalization or within 48 hours after discharge is called hospital-acquired pneumonia (HAP). Pneumonia that develops 48 hours after intubation in patients who do not have pneumonia during intubation is called ventilator-associated pneumonia (VAP).[21] HAP is the 2nd most common nosocomial infection in our country as well as in the whole world.[22]

When the diagnosis of HAP/VIP is made, empirical antibiotherapy should be initiated immediately. The evaluation of mortality risk factors and resistant infection risk factors in the selection of antibiotherapy and appropriate treatment is summarized in tables 11 and 12.[21]

Table 11. Empirical treatment of hospital-acquired pneumonia

In patients without risk factors for multidrug resistance	In cases with multidrug resistance risk and/or mortality risk*
Ceftazidime Cefepime Piperacillin - Tazobactam Cefoperazone - Sulbactam Imipenem Meropenem	Piperacillin - Tazobactam + Ciprofloxacin Cefoperazone - Sulbactam + Levofloxacin Imipenem** Amikacin Meropenem **

Table 12. Empirical treatment of ventilator-associated pneumonia

Standard treatment approach		
Piperacillin - Tazobactam Cefoperazone - Sulbactam Imipenem Meropenem Cefepime Ceftazidime	+	Ciprofloxacin or Levofloxacin Aminoglycoside Sulbactam Colistin *
Standard recommended treatment if Acinetobacter baumannii prevalence is high		
Cefoperazone - Sulbactam Imipenem Meropenem	+	Ciprofloxacin or Levofloxacin Aminoglycoside Sulbactam Colistin *

* One of Linezolid, Teicoplanin, or Vancomycin should be added to the treatment regimen of patients whose Gram-stained slides show Gram-positive cocci with staphylococcal morphology.

* A single risk factor may lead to unnecessary antibiotic use. Increasing the number of risk factors increases the likelihood of multidrug resistance.
* Colistin-containing combinations should be preferred in hospitals with a high prevalence of Gram-negative bacteria resistant to carbapenems.

High mortality risk factors include advanced age, two or more organ failures, the presence of a high APACHE score, underlying disease, bacteremia, late antibiotic initiation, and the need for mechanical ventilation.[21,23]

Risk factors for multidrug-resistant infection include IV antibiotic use within 90 days, the presence of septic

shock, hospitalization for 5 days or more before VAP, a history of acute renal replacement therapy, and the presence of ARDS before VAP.[23]

In both HAP and VAP, the recommended optimal duration of treatment for infections developing with susceptible pathogens whose causative agents are isolated and who do not have antibiotic resistance problems is 7 days on average. The determinant here is clinical, laboratory, and radiologic improvement.[23] In patients with MRSA growth, the optimal treatment is 14 days. In HAP caused by bacteria such as Acinetobacter, *Pseudomonas*, and *Stenotrophomonas*, the duration of treatment can again be extended to 14 days.[23]

COVID-19 PNEUMONIA

In late 2019, a new coronavirus called SARSCoV-2 (severe acute respiratory syndrome coronavirus) was identified in Wuhan province, China, with a severe pneumonia clinic. The disease, named COVID-19 by the World Health Organization, spread rapidly all over the world and in our country shortly after.

Clinical Findings

The disease can range from asymptomatic cases to acute respiratory distress syndrome. Patients with COVID-19 typically first progress from a mild upper respiratory tract infection (e.g., pharyngitis, runny nose) to a lower respiratory tract infection (e.g., cough, fever), flu-like symptoms (e.g., fever, chills, headache, myalgia), or gastroenteritis (e.g., nausea, vomiting, diarrhea). Loss of smell and taste may also occur, with loss of smell typically reported early in the disease. If dyspnea develops, it tends to occur four to eight days after the onset of symptoms, but it can also occur after 10 days. In addition, even where the prevalence of COVID-19 is high, the possibility of other symptom etiologies should be considered.[24]

Laboratory Findings

Common laboratory findings among COVID-19 patients include lymphopenia, elevated aminotransaminase levels, elevated lactate dehydrogenase levels, elevated inflammatory markers (for example, ferritin, C-reactive protein, and erythrocyte sedimentation rate), and abnormalities in coagulation tests (elevated D-dimer).

Imaging Findings

1.Chest radiographs: Chest radiographs may be normal in early or mild disease; common abnormal radiographic findings are consolidation and ground-glass opacities with bilateral, peripheral, and lower lung zone distributions; lung involvement increases over the course of the disease, with a peak in severity 10 to 12 days after symptom onset.

2.Thorax CT: Thoracic computed tomography (CT) is more sensitive than chest radiography. Some CT findings may be specific to COVID-19, but no finding can completely rule out the possibility of COVID-19.

Common CT findings:

*Ground glass opacifications

*Mixed consolidation frosted glass opacities

*Adjacent pleural thickening

*Interlobular septal thickening

*Expressed as air bronchograms.

Management in COVID-19 Patients

Direct detection of SARS-CoV-2 RNA, most frequently by reverse transcription polymerase chain reaction (RT-PCR), is the typical method for making the diagnosis of COVID-19 in patients with the aforementioned symptoms.

If the initial test is negative but suspicion of COVID-19 persists (e.g., suggestive symptoms without an obvious alternative cause) and confirmation of the presence of infection is important for management or infection control, PCR testing may be repeated.

Patients are assessed for previous chronic illnesses, smoking, and degree of dyspnea, and a decision is made whether to treat the patient on an outpatient or inpatient basis depending on the presence or absence of these conditions.

IMPORTANT POINTS

In patients with suspected pneumonia, chest radiography in the first 4 hours is effective in reducing mortality because it saves time in making the diagnosis. After the diagnosis of pneumonia is made, it is important to first determine the group to which the patient belongs and start appropriate empirical antibiotherapy. If possible, cultures should be taken before antibiotics are started on the patient for whom hospitalization is planned. After 72 hours, in patients with no symptom improvement, the reason for treatment non-response should be evaluated, and antibiotherapy should be changed if necessary.

ETHICAL DECLARATIONS

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Tabah A, Buetti N, Staiquly Q, et al. Epidemiology and outcomes of hospital-acquired bloodstream infections in intensive care unit patients: the EUROBACT-2 international cohort study. *Intensive Care Med*. 2023;*49*(2):178-190.
2. Cillóniz C, Torres A, Niederman MS. Management of pneumonia in critically ill patients. *BMJ*. 2021:375.
3. Metlay JP, Waterer GW, Long AC, et al. Diagnosis and treatment of adults with community-acquired pneumonia. An official clinical practice guideline of the American Thoracic Society and Infectious Diseases Society of America. *Am J Respirat Critic Care Med*. 2019;200(7):e45-e67.
4. Grabill N, Louis M, Idowu C, et al. Lung cavitation to pneumothorax: a case report of the multilayered respiratory challenges in oncology patients. *Internat J Surg Case Rep*. 2023:109157.
5. Gökırmak M, Hasanoğlu HC, Yıldırım Z, et al. Türk Toraks Derneği Pnömoni Rehberi'ne uygun tedavi verilen ve verilmeyen toplum kökenli pnömonilerde başarı oranları. 2001.
6. Musher DM, Roig IL, Cazares G, et al. Can an etiologic agent be identified in adults who are hospitalized for community-acquired pneumonia: results of a one-year study. *J Infect*. 2013;67(1):11-18.
7. Klompas M, Imrey PB, Yu PC, et al. Respiratory viral testing and antibacterial treatment in patients hospitalized with community-acquired pneumonia. *Infect Contr Hosp Epidemiol*. 2021:42(7):817-825.
8. Tapan ÖO, Tapan U. Tedavi rehberlerine uygun olarak hastaneye yatırılan ve tedavi edilen toplumda gelişen pnömonili yaşlı bireylerin klinik seyir ve tedavi başarısının değerlendirilmesi. *İzmir Göğüs Hasta Derg*. 2020;34(1):12-19.
9. Van der Lee L, Patman S, Hill AM. Development of a clinical practice guideline for physiotherapy management of adults invasively ventilated with community-acquired pneumonia. *Physiother*. 2023.
10. File Jr, T. M, Bartlett JG, Thorner AR. Treatment of community-acquired pneumonia in adults in the outpatient setting. 2015.
11. Jokinen C, Heiskanen L, Juvonen H, et al. Incidence of community-acquired pneumonia in the population of four municipalities in eastern Finland. *Am J Epidemiol*. 1993;137(9):977-988.
12. Guliyev U. D. E. K, Başyiğit İ. Solunum sistemi hastalıklarında semptomlar. Akciğer Hastalık Anamnez. 2023:39.
13. LA, Ismael PF, Alexandre TM, et al. Community-acquired pneumonia: epidemiology, diagnosis, prognostic severity scales, and new therapeutic options. *Medwave*. 2023;23(11):e2719-e2719. doi: 10.5867/medwave.2023.11.2719
14. Kilbert B, Kehr A, David Lim SY, et al. Effect of OMT on hospital length of stay in elderly patients with pneumonia: a meta-analysis. *Scholar: Pilot Validat Stud*. 2022;3(1):5-9.
15. Vivek Jayaschandran MD. Severity assessment of pneumonia. *World Clin Pulmon Crit Care Med: Pneumonia*. 2019;6.
16. Chongthanadon B, Thirawattanasoot N, Ruangsomboon O. Clinical factors associated with in-hospital mortality in elderly versus non-elderly pneumonia patients in the emergency department. *BMC Pulmon Med*. 2023;23(1):330.
17. Öğe N. Necmettin Erbakan Üniversitesi Meram Tıp Fakültesi Göğüs Hastalıkları Yoğun Bakım Ünitesi'nde entübe halde takip edilen pnömonili hastalarda bronkoalveolar lavaj ve trakeal aspiratmateryallerinin kültürlerinin ve gram boyamalarının kıyaslanması. 2023.
18. Şen P, Demirdal T, Nemli SA. Pnömokok İnfeksiyonlarının klinik özellikleri ve invazif hastalık göstergeleri. *Klimik Derg*. 2022;35(3):196-202.
19. Torumkuney D, Tunger A, Sancak B, et al. Results from the survey of antibiotic resistance (SOAR) 2015-2017 in Turkey: data based on CLSI, EUCAST (dose-specific) and pharmacokinetic/pharmacodynamic (PK/PD) breakpoints. *J Antimicrobi Chemotherap*. 2020;75(1):88-99.
20. Al-Jardani A, Al Rashdi A, Al Jaaidi A, et al. Serotype distribution and antibiotic resistance among invasive Streptococcus pneumoniae from Oman post 13-valent vaccine introduction. I*nternat J Infect Dis*. 2019;85:135-140.
21. Tapan ÖO, Tapan U. Tedavi rehberlerine uygun olarak hastaneye yatırılan ve tedavi edilen toplumda gelişen pnömonili yaşlı bireylerin klinik seyir ve tedavi başarısının değerlendirilmesi. *İzmir Göğüs Hast Derg*. 2020;34(1):12-19.
22. Balasar B, Ergün MÇ, Ergün B, Eroğlu E. Assessment of healthcare associated infections in a medical intensive care unit. *Dicle Tıp Derg*. 2023;311-318.
23. Shi Y, Huang Y, Zhang TT, et al. Chinese guidelines for the diagnosis and treatment of hospital-acquired pneumonia and ventilator-associated pneumonia in adults (2018 Edition). *J Thoracic Dis*. 2019;11(6):2581.
24. Dollard P, Griffin I, Berro A, et al. Risk assessment and management of COVID-19 among travelers arriving at designated US airports, January 17-September 13, 2020. *Morbidity Mortality Weekly Rep*. 2020;69(45):1681.
25. Wilson KC, Schoenberg NC, Cohn DL, et al. Community-acquired pneumonia guideline recommendations-impact of a consensus-based process versus systematic reviews. *Clinic Infect Dis*. 2021;73(7):1467-1475.