Severe Pneumonia

Patrick R. Ching, MD, MPH[a,b,*], Laura L. Pedersen, MD, MPH[a]

KEYWORDS

• Pneumonia • Critical illness • Intensive care unit • Hospitalization
• Community-acquired infections • COVID-19 • Therapeutics • Steroids

KEY POINTS

- Severe pneumonia is a life-threatening infection that requires intensive care.
- Samples from the respiratory tract and blood for cultures and molecular diagnostics obtained ideally before antimicrobial initiation aid in the identification of the pathogen and in targeted therapy.
- Antimicrobial therapy should be initiated early and tailored based on patient risk factors and local resistance data.
- Treatment with low-dose corticosteroids is associated with improved outcomes in severe pneumonia from bacteria, severe acute respiratory syndrome coronavirus 2, and *Pneumocystis jiroveci* (in people living with human immunodeficiency virus [HIV]).

INTRODUCTION

Pneumonia is an infection of the pulmonary parenchyma involving one or both the lungs. A leading cause of mortality and morbidity worldwide, severe community-acquired pneumonia (CAP), referred to as severe pneumonia from here on, is defined by the Infectious Diseases Society of America (IDSA) and the American Thoracic Society (ATS) as the presence of 1 major criterion (either requiring vasopressor support for shock or mechanical ventilation) or 3 or more minor criteria (**Box 1**).[1] This article reviews the most recent data on the epidemiology, microbiology, diagnosis, and management of severe pneumonia.

EPIDEMIOLOGY

In 2021, there were 344 million incident episodes of lower respiratory tract infections including pneumonia and bronchiolitis globally, excluding coronavirus disease 2019

[a] Division of Infectious Diseases, Department of Internal Medicine, Virginia Commonwealth University School of Medicine, 1000 East Marshall Street, Suite 107, Richmond, VA 23298, USA; [b] Healthcare Infection Prevention Program, Virginia Commonwealth University Health, Richmond, VA, USA
* Corresponding author.
E-mail address: patrick.ching1@vcuhealth.org
Twitter: @patrickching (P.R.C.)

Med Clin N Am 109 (2025) 705–720
https://doi.org/10.1016/j.mcna.2024.12.011 **medical.theclinics.com**
0025-7125/25/© 2024 Elsevier Inc. All rights are reserved, including those for text and data mining, AI training, and similar technologies.

Abbreviations

aOR	adjusted odds ratio
ARDS	acute respiratory distress syndrome
ATS	American Thoracic Society
CAP	community-acquired pneumonia
CI	confidence interval
COVID-19	coronavirus disease 2019
CRP	C-reactive protein
COPD	chronic obstructive pulmonary disease
DBP	diastolic blood pressure;
ESBL	extended spectrum beta lactamase
ESICM	European Society of Intensive Care Medicine
HIV	human immunodeficiency virus
ICU	intensive care unit
IDSA	Infectious Diseases Society of America
MDR	multidrug-resistant
MRSA	methicillin resistant *Staphylococcus aureus*
NIPPV	noninvasive positive pressure ventilation
PCT	procalcitonin
PSI	Pneumonia Severity Index
RCT	randomized controlled trials
RR	risk ratio
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
SBP	systolic blood pressure
VAP	ventilator-associated pneumonia
VILI	ventilator-induced lung injury

(COVID-19).[2] Of these, 2.18 million died, for an all-age mortality rate of 27.7 deaths per 100,000 population. Adults aged 70 years and older were the most affected (224.6 deaths per 100,000), followed by children younger than 5 years (76.2 deaths per 100,000).

In the United States, 23% of patients hospitalized with CAP required intensive care unit (ICU) admission, of whom 24% required invasive mechanical ventilation and 20%

Box 1
Severe community-acquired pneumonia criteria

Major Criteria
- Septic shock requiring vasopressors
- Respiratory failure requiring mechanical ventilation

Minor Criteria
- Confusion/disorientation
- Hypotension requiring fluid resuscitation
- Hypothermia <36°C
- Respiratory rate ≥30 breaths/min
- PaO_2/FiO_2 ≤250
- Blood urea nitrogen level ≥20 mg/dL
- Leukopenia due to infection alone <4000 cells/μL
- Thrombocytopenia <100,000 platelets/μL
- Multilobar infiltrates on imaging

Data from 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 Respir Crit Care Med. 2019;200(7):e45-e67. https://doi.org/10.1164/rccm.201908-1581ST.

required noninvasive ventilation.[3] The incidence of CAP in the ICU was 145 cases per 100,000 population, with a mortality rate of 27% at 30 days and 47% at 1 year.[3]

The cost of CAP is significant, with an estimated annual cost of $17 billion.[4] Severe pneumonia requiring ICU admission is associated with longer hospital stay (23.2 vs 9.1 days) and higher hospitalization cost ($21,144 vs $5785) compared with severe pneumonia without ICU use.[5] Hospital readmission was 12.5% during the 30-day postdischarge period and 42.3% during the 1-year postdischarge period.[6]

MICROBIOLOGY

Severe pneumonia can be caused by bacteria, viruses, or fungi. Bacterial pathogens are often separated into "typical" and "atypical" organisms. Typical organisms include *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Staphylococcus aureus*, and Gram-negative bacilli such as *Pseudomonas aeruginosa* and *Klebsiella pneumoniae*. Atypical organisms include *Legionella*, *Mycoplasma pneumoniae*, and *Chlamydia pneumoniae*. Respiratory syncytial virus (RSV), influenza, parainfluenza, adenovirus, and human metapneumovirus are viruses that can cause severe pneumonia. As seen during outbreaks, novel coronaviruses and influenza strains including the highly pathogenic avian influenza remain a significant concern given their potential for pandemic. Though less common, endemic fungi and molds can cause severe pneumonia usually in immunocompromised individuals. Polymicrobial infections occur in 10% to 15% of cases.

Bacterial Pathogens

Streptococcus pneumoniae is the most common bacterial cause of severe pneumonia.[7–9] Risk factors for development of severe pneumonia due to *S pneumoniae* include alcohol use disorder, tobacco smoking, chronic obstructive pulmonary disease (COPD), dementia, seizure disorders, heart failure, and cerebrovascular disorders.

Staphylococcus aureus pneumonia is more likely in persons with skin colonization or infection with *S aureus* and after viral infection. During the COVID-19 pandemic, *S aureus* was the most common bacterial pathogen present at the time of intubation.[10] Clinical presentation of pneumonia due to methicillin-sensitive *S aureus* is not different from methicillin-resistant *S aureus* (MRSA) pneumonia.[11] Though *S aureus* pneumonia remains relatively less common, its clinical outcomes are more severe than other types of CAP: longer hospital stay, higher ICU admission rate, more acute respiratory distress syndrome (ARDS), septic shock, and higher mortality.[11]

Pseudomonas aeruginosa is intrinsically resistant to multiple antibiotics. It tends to infect persons with structural lung disease such as cystic fibrosis, bronchiectasis, severe COPD, and chronic tracheostomy. It is an individual risk factor associated with mortality in CAP.[12]

Enterobacterales, an order of Gram-negative bacteria, is an important cause of severe pneumonia. Compared with patients with non-severe pneumonia, Enterobacterales are more frequently identified in patients with severe pneumonia. *Klebsiella pneumoniae* and *Escherichia coli* are among the most commonly isolated species.[13] Risk factors for Enterobacterales pneumonia include previous hospitalization, recent antibiotic use, aspiration, alcohol use disorder, heart failure, and renal failure. Known to include potentially multidrug-resistant (MDR) organisms, Enterobacterales can be extended-spectrum β-lactamase (ESBL)-producing or carbapenemase-resistant.

Atypical Pathogens

Atypical refers to the intrinsic resistance of these organisms to β-lactams and their inability to be visualized on Gram stain or cultured using traditional techniques. The

prevalence of severe pneumonia from atypical pathogens is 8.1%.[14] The most common of these is *Legionella pneumophila*, which causes Legionnaires' disease and is ubiquitous in freshwater habitats. *Legionella* can colonize man-made water systems and be dispersed by aerosols generated by showers, faucets, cooling towers, and fountains, causing disease outbreaks. Risk factors for *Legionella* pneumonia include malignancy, renal disease, diabetes mellitus, HIV infection, smoking, and recent hotel stay or trip on a cruise ship. *L pneumophila* has at least 16 serogroups but serogroup 1 is responsible for 84% of infections.[15]

Viral Pathogens

It is estimated that a third of all adult causes of CAP are due to viral infection.[16] Patients with severe pneumonia due to viruses are at risk for bacterial coinfection.[17]

Influenza is the most common cause of severe viral pneumonia. Seasonally occurring in the winter months, it carries a higher mortality among those in the extremes of age, pregnant and postpartum within 2 weeks, with chronic conditions such as metabolic disorder, neurologic conditions, and the immunocompromised. Annual influenza vaccination is available to prevent infection. For those who become ill, regardless of vaccination status, antiviral treatment with a single neuraminidase inhibitor should be administered for hospitalized patients, outpatients with progressive disease, individuals at risk for developing severe disease, or anyone with illness <48 hours of duration.[18]

RSV is the second most common cause of viral pneumonia in adults. It typically causes acute upper respiratory tract infection; nevertheless, infants under 6 months of age and children with the following risk factors can develop severe RSV pneumonia: prematurity, immunocompromised, neuromuscular disorders, congenital abnormalities, and severe cystic fibrosis. Adults at least age 75 years or 60 to 74 years with the following conditions are at increased risk for severe RSV pneumonia: cardiovascular disease, pulmonary disease, end-stage renal disease, liver disease, hematologic conditions, diabetes mellitus with end-organ damage or requiring insulin and/or sodium-glucose cotransporter-2 inhibitor, a body mass index $\geq$40 kg/m^2, moderate to severe immunocompromised state, a neurologic condition that affects airway clearance or respiratory muscle use, and residence in a congregate living facility. Though treatment is largely supportive, in patients who are severely immunocompromised particularly hematopoietic stem cell transplant recipients with severe RSV pneumonia, ribavirin may be considered.[19] Three vaccines to prevent severe lower respiratory tract disease caused by RSV in adults are approved by the United States Food and Drug Administration. For infants and children, a prenatal vaccine for the mother or RSV antibody given to the child can prevent RSV pneumonia.[20]

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a novel virus that causes COVID-19. It is estimated that the pandemic resulted in 15 million excess deaths globally in 2020 to 2021.[21] Risk factors for severe COVID-19, defined as having hypoxemia (oxygen saturation $\leq$94% on room air) including those on supplemental oxygen or ventilatory support,[22] include age $\geq$65 years, chronic lung disease, diabetes mellitus, malignancy, cardiovascular disease, obesity, and immunosuppression. Remdesivir, tocilizumab, barcitinib, and corticosteroids are therapies for severe COVID-19 pneumonia. Before the SARS-CoV-2 pandemic, 2 other coronaviruses—severe acute respiratory syndrome coronavirus 1 and Middle East respiratory syndrome coronavirus—caused severe viral pneumonia.

Fungal Pathogens

Aspergillus, *Cryptococcus*, *Pneumocystis*, and endemic fungi (*Histoplasma capsulatum*, *Blastomyces dermatiditis*, *Coccidioides immitis*) are the major pathogens of

severe fungal pneumonia. *Candida* very rarely causes pneumonia because invasion of pulmonary tissue is rare; its isolation in respiratory cultures typically represent colonization. Fungal pneumonia tends to occur in immunocompromised hosts, particularly those with CD4+ T-cell deficiencies. This includes people living with HIV, those with prolonged and profound neutropenia, bone marrow and organ transplant recipients, individuals with hematologic malignancies, or conditions requiring immunosuppressive medications such as corticosteroids. Those with chronic organ dysfunction such as cirrhosis, end-stage renal disease, and chronic lung disease are also at risk. Fungal pneumonia can be a complication of severe COVID-19. Amphotericin B is used for treatment of endemic mycoses and resistant fungi. Azole antifungals such as voriconazole, isavuconazole, or posaconazole are used for *Aspergillus* infections.

CLINICAL MANIFESTATIONS

Severe pneumonia usually presents with constitutional findings and signs and symptoms attributable to the lungs and associated structures. Patients can have high fever, intense chills, sweats, and/or cough productive of mucoid, purulent, or blood-tinged sputum. They can feel short of breath and/or pleuritic chest pain. Other systemic symptoms may include fatigue, headache, myalgia, or arthralgia. Particularly in older adults, confusion or changes in mental status can be seen.

On physical examination, patients can have tachycardia, tachypnea, and hypotension. Hypoxia is usually severe. Temperature can be extremes: very high or very low. Septic shock and evidence of end-organ failure are common. Crackles and bronchial breath sounds may be heard.

DIAGNOSIS

Sputum or lower respiratory tract cultures and blood cultures should be obtained in patients with severe pneumonia, ideally before antimicrobial initiation. Early acquisition of these specimens ensures optimal sensitivity. Comprehensive metabolic panel and complete blood count are used in the case definition and risk stratification of potential severe pneumonia. *Legionella* urinary antigen test, which only detects serogroup 1, may especially be useful in cases where relevant epidemiologic factors are present. Chest radiographic findings may show multifocal consolidation, infiltrates, and/or pleural effusion. Cavitation and multilobar involvement may suggest increased severity. Computed tomography of the chest may be helpful in cases when chest radiograph results are uncertain.

Molecular Diagnostics

Nucleic acid amplification tests of respiratory samples provide rapid results with excellent sensitivity. Polymerase chain reaction (PCR) assays that detect SARS-CoV-2, influenza A and B, RSV, and other respiratory viruses inform isolation precautions and initiation of therapy for severe COVID-19 and other viruses treatable with antivirals. Though bacterial superinfection may be difficult to distinguish from primary severe viral pneumonia, a positive viral detection in the absence of a bacterial infection could help in antibiotic de-escalation.

Multiplex PCR panels can also detect bacterial pathogens and resistance genes such as atypicals, MRSA, MDR and non-MDR *Pseudomonas*, ESBL-producing and carbapenem-resistant Enterobacterales, and *Acinetobacter*. They can particularly be useful in the presence of new or worsening lung infiltrates, receipt of empiric antibiotics prior to obtaining cultures, and/or if there is concern for MDR organism or

polymicrobial infection. Antimicrobial therapy can be rapidly adjusted for unsuspected antibiotic-resistant pathogens, decreasing the duration of inappropriate antimicrobial use.[23] Single-target or multiplex PCR assays for detection of *mec*A gene which confers methicillin-resistance can exclude MRSA pneumonia. Given the excellent negative predictive value of MRSA nasal swab for MRSA pneumonia,[24] anti-MRSA therapy can be safely discontinued even in critically ill patients with severe pneumonia.

Biomarkers

Procalcitonin (PCT) and C-reactive protein (CRP) are 2 commonly used biomarkers in severe pneumonia. As acute-phase reactants, their levels rise in the presence of an inflammatory response, particularly to bacterial pathogens: PCT at day 1 after symptom onset while CRP at day 3 after symptom onset.[25] Nevertheless, they should not be used to decide initiation of antibiotics, regardless of initial level. In conjunction with clinical judgment, PCT can be measured serially to guide reduction in antibiotic therapy duration,[26–28] which is associated with decreased mortality.[29]

Severity Stratification

Validated clinical prediction tools are used in the evaluation of patients presenting with pneumonia. Developed to predict mortality, they help in the determination of illness severity together with clinical judgment. Pneumonia Severity Index (PSI) and the CURB-65 are the most frequently used tools. PSI stratifies patients into 5 tiers based on patient age, comorbidities, physical examination findings, laboratory abnormalities, and imaging findings (**Fig. 1** and **Table 1**).[30] CURB-65 is simpler and based on 5

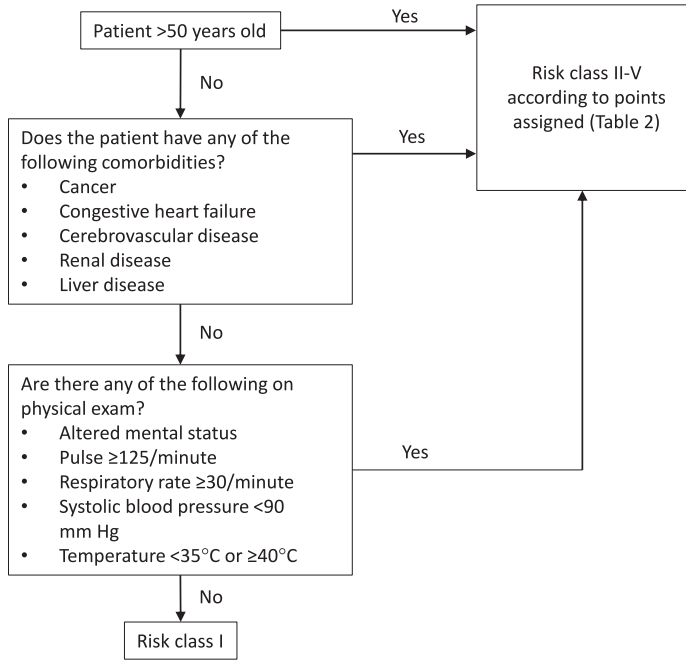

Fig. 1. Initial algorithm for Pneumonia Severity Index for a patient with a diagnosis of pneumonia. (*Data from* Fine MJ, Auble TE, Yealy DM, et al. A prediction rule to identify low-risk patients with community-acquired pneumonia. N Engl J Med 1997;336(4):243-250. https://doi.org/10.1056/NEJM199701233360402.)

Table 1
Point scoring system for prediction rule for assignment to risk classes II, III, IV, and V and the risk category based on total points

Characteristic	Points Assigned
Demographic	
Age	
Men	Age (y)
Women	Age (y)-10
Nursing home resident	+10
Comorbidities	
Cancer (excluding basal or squamous cell carcinoma of the skin)	+30
Liver disease	+20
Congestive heart failure	+10
Cerebrovascular disease	+10
Chronic kidney disease	+10
Physical Examination Findings	
Altered mentation	+20
Respiratory rate ≥30 breaths/min	+20
Systolic blood pressure <90 mm Hg	+20
Temperature ≤95°F or ≥104°F	+15
Pulse ≥125 beats/min	+10
Laboratory and Radiographic Findings	
Arterial pH <7.35	+30
Blood urea nitrogen >30 mg/dL	+20
Sodium <130 mmol/L	+20
Glucose >250 mg/dL	+10
Hematocrit <30%	+10
Partial pressure of arterial oxygen <60 mm Hg	+10
Pleural effusion	+10

Risk Class and Mortality Based on Cumulative Number of Points[a]

Class	Cumulative Points	30-d Mortality Risk[b]
I[c]	N/A	0.10%
II	≤70	0.60%
III	71–90	0.90%
IV	91–130	9.3%
V	>130	27%

[a] *Data from* Fine M, Auble T, Yealy D, et al. A prediction rule to identify low-risk patients with community-acquired pneumonia. N Engl J Med 1997;336(4):243-250. https://doi.org/10.1056/NEJM199701233360402.
[b] *Data from* Seymann G, Barger K, Choo S, et al. Clinical judgment versus the Pneumonia Severity Index in making the admission decision. J Emerg Med 2008;34(3):261-268. https://doi.org/10.1016/j.jemermed.2007.05.050.
[c] Age <50 y; no cancer, congestive heart failure, renal, liver, or cerebrovascular disease with normal vital signs and mentation.

Table 2
CURB-65

Criterion	
Confusion	
Urea >19.6 mg/dL	
Respiratory rate >30 breaths/min	
Blood pressure SBP <90 mm Hg or DBP ≤60 mm Hg	
Age ≥65 y	
Score	**Mortality Risk**
0–1	1.5% (low)
2	9.2% (intermediate)
≥3	22% (high)

Each criterion is assigned a score of 1.

Abbreviations: DBP, diastolic blood pressure; SBP, systolic blood pressure.

Data from Lim W, van der Eerden M, Laing R, et al. Defining community acquired pneumonia severity on presentation to hospital: an international derivation and validation study. Thorax. 2003;58(5):377-382. https://doi.org/10.1136/thorax.58.5.377.

criteria: confusion, blood urea nitrogen, respiratory rate, blood pressure, and age (**Table 2**).[31]

The PSI is preferred over the CURB-65. Though it may underestimate illness severity in younger populations, the PSI has a higher discriminative power in predicting mortality compared with CURB-65.[32] In general, patients in PSI classes I-III have a predicted 30-day mortality of <1% and thus can be managed as outpatient unless contraindications are present.[33] Factors such as cognitive status, impaired functionality, severe comorbid conditions, psychiatric illness, and substance use disorder are considered in determining the need for hospitalization.[34,35] The CURB-65 and the PSI were not designed to assist in determining the level of care for a hospitalized patient. Patients who require vasopressors or mechanical ventilation should be directly admitted to the ICU. For remaining hospitalized patients, clinical judgment and the type of minor criteria met should be considered (see **Box 1**). Late admission of patients with severe pneumonia to the ICU is associated with increased mortality.[36]

MANAGEMENT

The management of severe pneumonia involves both antimicrobial and nonantimicrobial therapies. While antimicrobials are the mainstay of therapy, adjunctive nonantimicrobial therapies are associated with better survival.

Antimicrobial Therapy

Antimicrobial treatment for patients hospitalized with severe pneumonia should be tailored based on risk factors and local resistance data. Generally, the empiric therapy is a combination of a β-lactam and a macrolide. β-lactam covers *S. pneumoniae* and other common respiratory pathogens while macrolide covers atypical pathogens. The 2019 IDSA/ATS guidelines recommend either a macrolide or a fluoroquinolone for atypical coverage,[1] whereas the 2022 European Respiratory Society, European Society of Intensive Care Medicine (ESICM), European Society of Clinical Microbiology and Infectious Diseases, and Latin American Thoracic Association suggest macrolides over fluoroquinolones. Though there are no randomized controlled trials (RCTs)

comparing macrolides and fluoroquinolones, observational studies showed more frequent mortality reduction in patients who received macrolides instead of fluoroquinolones. In a meta-analysis of 28 observational studies including 9850 patients, macrolide use was associated with lower mortality compared with nonmacrolide use (risk ratio [RR] 0.82, 95% confidence interval [CI] 0.70–0.97).[37] A prospective cohort study of hospitalized patients with CAP showed a combination of β-lactam and macrolide reduced mortality in patients with pneumococcal CAP and high inflammatory response (CRP >15 mg/dL) (adjusted odds ratio [aOR] 0.28, 95% CI 0.09–0.93).[38] Macrolides not only have antibacterial properties but also have anti-inflammatory activity which could be beneficial in patients with severe pneumonia.

If there are risk factors for *P aeruginosa* infection, antipseudomonal β-lactam such as piperacillin-tazobactam, cefepime, ceftazidime, or meropenem should be started. If MRSA pneumonia is considered, the regimen should include an anti-MRSA agent such as vancomycin. Risk factors for respiratory infection with *P aeruginosa* or MRSA are prior isolation of these organisms, hospitalization, and parenteral antibiotic exposure in the last 90 days.[1] Empiric treatment of hospital-acquired pneumonia or ventilator-associated pneumonia (VAP) should include antipseudomonal and anti-MRSA coverage. Adjustment of antimicrobial therapy based on microbiologic data reduces exposure to antimicrobials, length of stay (risk-adjusted ratio of means 0.76, 95% CI 0.75–0.78), and hospitalization cost (risk-adjusted ratio of means 0.74, 95% CI 0.72–0.76).[39]

Nonantimicrobial Therapies

Nonantimicrobial therapies for severe pneumonia are directed to the host response rather than the microorganism. These interventions improve clinical outcomes and include systemic corticosteroids and lung-protective ventilation strategy.

Systemic corticosteroids

Corticosteroids mitigate the regional and systemic immune and inflammatory response to severe pulmonary infection. Though previous RCTs[40,41] showed that high-dose corticosteroids were not beneficial for treatment of critically ill patients with septic shock, more recent studies involving lower doses of corticosteroids (less than or equal to hydrocortisone 400 mg equivalent daily) suggest otherwise.

In patients with severe bacterial pneumonia, low-dose corticosteroids are beneficial. In a meta-analysis including 17 RCTs involving 2264 patients, low-dose corticosteroids were associated with reduced mortality in adults with severe CAP (RR 0.58; 95% CI 0.40–0.84).[42] Majority of the trials used doses equivalent to hydrocortisone 160 to 200 mg daily, started between 12 and 36 hours after hospital admission for 5 to 10 days. In an individual patient data meta-analysis of 6 studies with 1506 patients, low-dose corticosteroids typically initiated within 36 hours of admission reduced time to clinical stability (−1.03 days; 95% CI −1.62 to −0.43) and length of hospital stay (−1.15 days; 95% CI −1.75 to −0.55) but were not associated with mortality reduction (aOR 0.75; 95% CI 0.46–1.21).[43] It was based on these data that the 2019 IDSA/ATS guidelines recommended against corticosteroids.[1] However, a recent meta-analysis of 7 RCTs of 1689 patients with severe CAP who received hydrocortisone dose equivalent ≤400 mg daily for ≤8 days demonstrated a decreased 30-day mortality in the low-dose corticosteroid group compared to the placebo group (RR 0.61; 95% CI 0.44–0.85).[44] Low-dose corticosteroids were also associated with a lower risk of requirement of mechanical ventilation (RR 0.57; 95% CI 0.45–0.73) and shorter length of ICU stay (mean difference −0.8; 95% CI −1.4 to −0.1) and hospital stay (mean difference −1.1; 95% CI, −2.0 to −0.1).[44] Additionally, in a prespecified subgroup

analysis of an RCT of patients with CAP and septic shock, hydrocortisone plus fludrocortisone reduced mortality compared with placebo (OR 0.60; 95% CI 0.43–0.83).[45] According to these data, low-dose corticosteroids are recommended for patients with severe community-acquired bacterial pneumonia.

Patients with COVID-19 requiring supplemental oxygen benefit from low-dose corticosteroids. A meta-analysis including 7 RCTs involving 1703 critically ill patients with COVID-19 showed a decline in mortality among those who received dexamethasone (OR 0.64; 95% CI 0.50–0.82).[46] However, since corticosteroids did not decrease mortality in patients with COVID-19 who did not require supplemental oxygen,[47,48] they are not recommended for outpatients and those who are hospitalized but do not require supplemental oxygen.

Low-dose corticosteroids are beneficial to people living with HIV and moderate to severe *Pneumocystis jiroveci* pneumonia (arterial oxygen partial pressure <70 mm Hg or an alveolar-arterial gradient >35 mmHg on room air). A meta-analysis including 6 RCTs with 489 patients showed that use of low-dose corticosteroids decreased mortality at 1 month (RR 0.56; 95% CI, 0.32–0.98) and at 3 to 4 months of follow-up (RR 0.59; 95% CI, 0.41–0.85).[49]

Lung-protective ventilation strategy

Severe pneumonia is a major cause of ARDS. Ventilator-induced lung injury (VILI) is one of the most common complications of mechanical ventilation. It activates systemic inflammation, induces multiorgan failure, and increases mortality. Lung-protective ventilation strategy which includes using lower tidal volumes, lower inspiratory pressures (plateau pressure <30 cm H_2O), and prone positioning may alleviate VILI and improve clinical outcomes. A meta-analysis of 11 RCTs including 1795 patients showed that use of lower tidal volume (4–8 mL/kg predicted body weight) reduced mortality risk in patients with ARDS compared with higher tidal volumes (>8 mL/kg predicted body weight) (RR 0.79; 95% CI 0.66–0.94).[50] Prone positioning for >12 hours/d reduced mortality in a subgroup of 1002 patients with moderate to severe ARDS from 5 trials (RR 0.74, 95% CI 0.56–0.99) included in a meta-analysis.[51] The ATS, ESICM, and Society of Critical Care Medicine recommend lung-protective ventilation strategy in adult patients with ARDS, including those with severe pneumonia.[52]

PREVENTION

In the community, pneumonia in its severe form can be prevented by vaccination and avoidance of tobacco smoke. Pneumococcal, influenza, and COVID-19 vaccines as well as vaccines for *Haemophilus influenzae* type B, pertussis, varicella, and measles can all help prevent pneumonia and other complications of these infections. Exposure to tobacco smoke is associated with increased risk of pneumonia. Compared to those who never smoked, current smokers (pooled OR 2.17; 95% CI 1.70–2.76) and previous smokers (pooled OR 1.49; 95% CI 1.26–1.75) are more likely to develop pneumonia.[53] On the other hand, 5 years of smoking cessation was associated with 50% reduction in the risk of pneumonia.[54]

Hospitalized patients are especially at high risk for pneumonia. The following are essential practices in hospitals recommended by expert societies to prevent severe pneumonia that require mechanical ventilation.[55] Semirecumbent position—elevating the head of the bed to 30° to 45° (up to 60°)—decreases the risk of VAP compared to a supine position.[56] Daily toothbrushing is associated with lower VAP rates,[57,58] shorter duration of mechanical ventilation, and shorter ICU stay.[58] Though the impact of routine oral care with chlorhexidine on VAP rates remains unclear, meta-analyses of

RCTs[59–61] and a cohort study[62] show increased mortality with chlorhexidine oral care and it is not recommended. Early enteral nutrition showed a reduction in hospital-acquired pneumonia and shorter ICU and hospital stay compared to early parenteral nutrition.[63]

Use of high-flow nasal oxygen or noninvasive positive pressure ventilation (NIPPV) as appropriate may avoid intubation and reintubation in critically ill patients. Compared to standard oxygen therapy, NIPPV is associated with decreased risk of VAP[64] and mortality.[65–68] Sedation should be minimized as much as possible in ventilated patients without contraindication. Protocols for minimizing sedation, daily sedation interruptions, and ventilation liberation are associated with shorter ICU stay.[69,70] Favoring the use of multimodal strategies and nonbenzodiazepine medications such as reassurance for anxiety, analgesics for pain, and dexmedetomidine and/or propofol for agitation are also associated with shorter time to extubation and ICU stay.[71] Maintenance and improvement of physical conditioning through early exercise and mobilization are associated with lower risk of VAP[72,73] and shorter duration of mechanical ventilation.[69,72,74]

SUMMARY

Severe pneumonia is a lung infection associated with high morbidity and mortality. It occurs more commonly in older adults with chronic comorbidities, impaired airway protection, tobacco use disorder, and alcohol use disorder. Caused by bacteria, viruses, or fungi, it is diagnosed based on clinical presentation and radiologic findings. Intensive care and early initiation of antibiotics are required as delays and inadequacies in care lead to poor outcomes. Rapid and accurate diagnostic tests that detect pathogens and antimicrobial resistance aid in targeted therapy. Adjunctive corticosteroids are associated with decreased mortality and should be considered.

CLINICS CARE POINTS

- Molecular diagnostics such as PCR testing yield rapid results and are highly sensitive. Caution must be exercised in interpreting results as they could represent colonization and not infection.
- Pneumonia scoring systems such as PSI and CURB-65 were developed to estimate mortality risk and not to determine the level of care for a hospitalized patient. They must always be used with clinical judgment.
- Procalcitonin and C-reactive protein, regardless of level, are never used to determine initiation of antimicrobial therapy for pneumonia.
- Fungal pneumonia should be a consideration if there is unresolved pneumonia despite antibacterial therapy.
- Radiologic improvement often lags behind clinical improvement in pneumonia.

DISCLOSURES

The authors have nothing to disclose.

REFERENCES

1. 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 Respir Crit Care Med 2019;200(7):e45–67.
2. GBD 2021 Lower Respiratory Infections and Antimicrobial Resistance Collaborators. Global, regional, and national incidence and mortality burden of non-COVID-19 lower respiratory infections and aetiologies, 1990-2021: a systematic analysis from the Global Burden of Disease Study 2021. Lancet Infect Dis 2024;24(9):974–1002.
3. Cavallazzi R, Furmanek S, Arnold FW, et al. The burden of community-acquired pneumonia requiring admission to ICU in the United States. Chest 2020;158(3):1008–16.
4. File TM, Marrie TJ. Burden of community-acquired pneumonia in North American adults. Postgrad Med 2010;122(2):130–41.
5. Angus DC, Marrie TJ, Obrosky DS, et al. Severe community-acquired pneumonia: use of intensive care services and evaluation of American and British Thoracic Society diagnostic criteria. Am J Respir Crit Care Med 2002;166(5):717–23.
6. Averin A, Shaff M, Weycker D, et al. Mortality and readmission in the year following hospitalization for pneumonia among US adults. Respir Med 2021;185:106476.
7. Qu J, Zhang J, Chen Y, et al. Aetiology of severe community acquired pneumonia in adults identified by combined detection methods: a multi-centre prospective study in China. Emerg Microbes Infect 2022;11(1):556–66.
8. Song JH, Huh K, Chung DR. Community-acquired pneumonia in the Asia-Pacific region. Semin Respir Crit Care Med 2016;37(6):839–54.
9. Cilloniz C, Ferrer M, Liapikou A, et al. Acute respiratory distress syndrome in mechanically ventilated patients with community-acquired pneumonia. Eur Respir J 2018;51(3):1702215.
10. Pickens CO, Gao CA, Cuttica MJ, et al. Bacterial superinfection pneumonia in patients mechanically ventilated for COVID-19 pneumonia. Am J Respir Crit Care Med 2021;204(8):921–32.
11. Self WH, Wunderink RG, Williams DJ, et al. Staphylococcus aureus community-acquired pneumonia: prevalence, clinical characteristics, and outcomes. Clin Infect Dis 2016;63(3):300–9.
12. Cillóniz C, Gabarrús A, Ferrer M, et al. Community-acquired pneumonia due to multidrug- and non-multidrug-resistant Pseudomonas aeruginosa. Chest 2016;150(2):415–25.
13. Villafuerte D, Aliberti S, Soni NJ, et al. Prevalence and risk factors for Enterobacteriaceae in patients hospitalized with community-acquired pneumonia. Respirology 2020;25(5):543–51.
14. Wang S, Tang J, Tan Y, et al. Prevalence of atypical pathogens in patients with severe pneumonia: a systematic review and meta-analysis. BMJ Open 2023;13(4):e066721.
15. Yu VL, Plouffe JF, Pastoris MC, et al. Distribution of Legionella species and serogroups isolated by culture in patients with sporadic community-acquired legionellosis: an international collaborative survey. J Infect Dis 2002;186(1):127–8.
16. Ruuskanen O, Lahti E, Jennings LC, et al. Viral pneumonia. Lancet 2011;377(9773):1264–75.
17. Melamed KH, Williams J, Wang X, et al. Development of secondary bacterial pneumonia in adults presenting with influenza versus noninfluenza viral respiratory infection. Ther Adv Respir Dis 2020;14:1753466620963026.

18. Uyeki TM, Bernstein HH, Bradley JS, et al. Clinical practice guidelines by the Infectious Diseases Society of America: 2018 update on diagnosis, treatment, chemoprophylaxis, and institutional outbreak management of seasonal influenza. Clin Infect Dis 2019;68(6):895–902.
19. Manothummetha K, Mongkolkaew T, Tovichayathamrong P, et al. Ribavirin treatment for respiratory syncytial virus infection in patients with haematologic malignancy and haematopoietic stem cell transplant recipients: a systematic review and meta-analysis. Clin Microbiol Infect 2023;29(10):1272–9.
20. Centers for Disease Control and Prevention. Respiratory syncytial virus (RSV) - RSV in infants and young children. Available at: https://www.cdc.gov/rsv/high-risk/infants-young-children.html. Accessed October 29, 2024.
21. Msemburi W, Karlinsky A, Knutson V, et al. The WHO estimates of excess mortality associated with the COVID-19 pandemic. Nature 2023;613(7942):130–7.
22. Bhimraj A, Morgan RL, Shumaker AH, et al. Infectious Diseases Society of America guidelines on the treatment and management of patients with COVID-19 (September 2022). Clin Infect Dis 2024;78(7):e250–349.
23. Darie AM, Khanna N, Jahn K, et al. Fast multiplex bacterial PCR of bronchoalveolar lavage for antibiotic stewardship in hospitalised patients with pneumonia at risk of Gram-negative bacterial infection (Flagship II): a multicentre, randomised controlled trial. Lancet Respir Med 2022;10(9):877–87.
24. Parente DM, Cunha CB, Mylonakis E, et al. The clinical utility of methicillin-resistant Staphylococcus aureus (MRSA) nasal screening to rule out MRSA pneumonia: a diagnostic meta-analysis with antimicrobial stewardship implications. Clin Infect Dis 2018;67(1):1–7.
25. Méndez R, Menéndez R, Cillóniz C, et al. Initial inflammatory profile in community-acquired pneumonia depends on time since onset of symptoms. Am J Respir Crit Care Med 2018;198(3):370–8.
26. Bouadma L, Luyt CE, Tubach F, et al. Use of procalcitonin to reduce patients' exposure to antibiotics in intensive care units (PRORATA trial): a multicentre randomised controlled trial. Lancet 2010;375(9713):463–74.
27. de Jong E, van Oers JA, Beishuizen A, et al. Efficacy and safety of procalcitonin guidance in reducing the duration of antibiotic treatment in critically ill patients: a randomised, controlled, open-label trial. Lancet Infect Dis 2016;16(7):819–27.
28. Kyriazopoulou E, Liaskou-Antoniou L, Adamis G, et al. Procalcitonin to reduce long-term infection-associated adverse events in sepsis. A randomized trial. Am J Respir Crit Care Med 2021;203(2):202–10.
29. Pepper DJ, Sun J, Rhee C, et al. Procalcitonin-guided antibiotic discontinuation and mortality in critically ill adults: a systematic review and meta-analysis. Chest 2019;155(6):1109–18.
30. Fine M, Auble T, Yealy D, et al. A prediction rule to identify low-risk patients with community-acquired pneumonia. N Engl J Med 1997;336(4):243–50.
31. Lim W, van der Eerden M, Laing R, et al. Defining community acquired pneumonia severity on presentation to hospital: an international derivation and validation study. Thorax 2003;58(5):377–82.
32. Aujesky D, Auble TE, Yealy DM, et al. Prospective comparison of three validated prediction rules for prognosis in community-acquired pneumonia. Am J Med 2005;118(4):384–92.
33. Seymann G, Barger K, Choo S, et al. Clinical judgment versus the Pneumonia Severity Index in making the admission decision. J Emerg Med 2008;34(3):261–8.

34. Marrie TJ, Huang JQ. Low-risk patients admitted with community-acquired pneumonia. Am J Med 2005;118(12):1357–63.
35. Labarere J, Stone RA, Scott Obrosky D, et al. Factors associated with the hospitalization of low-risk patients with community-acquired pneumonia in a cluster-randomized trial. J Gen Intern Med 2006;21(7):745–52.
36. Restrepo MI, Mortensen EM, Rello J, et al. Late admission to the ICU in patients with community-acquired pneumonia is associated with higher mortality. Chest 2010;137(3):552–7.
37. Sligl WI, Asadi L, Eurich DT, et al. Macrolides and mortality in critically ill patients with community-acquired pneumonia: a systematic review and meta-analysis. Crit Care Med 2014;42(2):420–32.
38. Ceccato A, Cilloniz C, Martin-Loeches I, et al. Effect of combined β-lactam/macrolide therapy on mortality according to the microbial etiology and inflammatory status of patients with community-acquired pneumonia. Chest 2019;155(4):795–804.
39. Deshpande A, Richter SS, Haessler S, et al. De-escalation of empiric antibiotics following negative cultures in hospitalized patients with pneumonia: rates and outcomes. Clin Infect Dis 2021;72(8):1314–22.
40. Sprung CL, Caralis PV, Marcial EH, et al. The effects of high-dose corticosteroids in patients with septic shock. A prospective, controlled study. N Engl J Med 1984;311(18):1137–43.
41. Bone RC, Fisher CJ, Clemmer TP, et al. A controlled clinical trial of high-dose methylprednisolone in the treatment of severe sepsis and septic shock. N Engl J Med 1987;317(11):653–8.
42. Stern A, Skalsky K, Avni T, et al. Corticosteroids for pneumonia. Cochrane Database Syst Rev 2017;2017(12). https://doi.org/10.1002/14651858.CD007720.pub3.
43. Briel M, Spoorenberg SMC, Snijders D, et al. Corticosteroids in patients hospitalized with community-acquired pneumonia: systematic review and individual patient data metaanalysis. Clin Infect Dis 2018;66(3):346–54.
44. Wu JY, Tsai YW, Hsu WH, et al. Efficacy and safety of adjunctive corticosteroids in the treatment of severe community-acquired pneumonia: a systematic review and meta-analysis of randomized controlled trials. Crit Care 2023;27(1):274.
45. Heming N, Renault A, Kuperminc E, et al. Hydrocortisone plus fludrocortisone for community acquired pneumonia-related septic shock: a subgroup analysis of the APROCCHSS phase 3 randomised trial. Lancet Respir Med 2024;12(5):366–74.
46. WHO Rapid Evidence Appraisal for COVID-19 Therapies (REACT) Working Group, Sterne JAC, Murthy S, et al. Association between administration of systemic corticosteroids and mortality among critically ill patients with COVID-19: a meta-analysis. JAMA 2020;324(13):1330–41.
47. RECOVERY Collaborative Group, Horby P, Lim WS, et al. Dexamethasone in hospitalized patients with Covid-19. N Engl J Med 2021;384(8):693–704.
48. Crothers K, DeFaccio R, Tate J, et al. Dexamethasone in hospitalised COVID-19 patients not on intensive respiratory support. Eur Respir J 2022;60(1):2102532.
49. Ewald H, Raatz H, Boscacci R, et al. Adjunctive corticosteroids for Pneumocystis jiroveci pneumonia in patients with HIV infection. Cochrane Database Syst Rev 2015;2015(4):CD006150.
50. Yamamoto R, Okazaki SR, Fujita Y, et al. Usefulness of low tidal volume ventilation strategy for patients with acute respiratory distress syndrome: a systematic review and meta-analysis. Sci Rep 2022;12(1):9331.

51. Munshi L, Del Sorbo L, Adhikari NKJ, et al. Prone position for acute respiratory distress syndrome: a systematic review and meta-analysis. Ann Am Thorac Soc 2017;14(Supplement_4):S280–8.
52. Fan E, Del Sorbo L, Goligher EC, et al. An official American Thoracic Society/European Society of Intensive Care Medicine/Society of Critical Care Medicine clinical practice guideline: mechanical ventilation in adult patients with acute respiratory distress syndrome. Am J Respir Crit Care Med 2017;195(9):1253–63.
53. Baskaran V, Murray RL, Hunter A, et al. Effect of tobacco smoking on the risk of developing community acquired pneumonia: a systematic review and meta-analysis. PLoS One 2019;14(7):e0220204.
54. Almirall J, González CA, Balanzó X, et al. Proportion of community-acquired pneumonia cases attributable to tobacco smoking. Chest 1999;116(2):375–9.
55. Klompas M, Branson R, Cawcutt K, et al. Strategies to prevent ventilator-associated pneumonia, ventilator-associated events, and nonventilator hospital-acquired pneumonia in acute-care hospitals: 2022 update. Infect Control Hosp Epidemiol 2022;43(6):687–713.
56. Wang L, Li X, Yang Z, et al. Semi-recumbent position versus supine position for the prevention of ventilator-associated pneumonia in adults requiring mechanical ventilation. Cochrane Database Syst Rev 2016;2016(1):CD009946.
57. Zhao T, Wu X, Zhang Q, et al. Oral hygiene care for critically ill patients to prevent ventilator-associated pneumonia. Cochrane Database Syst Rev 2020;12(12):CD008367.
58. Sozkes S, Sozkes S. Use of toothbrushing in conjunction with chlorhexidine for preventing ventilator-associated pneumonia: a random-effect meta-analysis of randomized controlled trials. Int J Dent Hyg 2023;21(2):389–97.
59. Price R, MacLennan G, Glen J, SuDDICU Collaboration. Selective digestive or oropharyngeal decontamination and topical oropharyngeal chlorhexidine for prevention of death in general intensive care: systematic review and network meta-analysis. BMJ 2014;348:g2197.
60. Klompas M, Speck K, Howell MD, et al. Reappraisal of routine oral care with chlorhexidine gluconate for patients receiving mechanical ventilation: systematic review and meta-analysis. JAMA Intern Med 2014;174(5):751–61.
61. Klompas M, Li L, Kleinman K, et al. Associations between ventilator bundle components and outcomes. JAMA Intern Med 2016;176(9):1277–83.
62. Deschepper M, Waegeman W, Eeckloo K, et al. Effects of chlorhexidine gluconate oral care on hospital mortality: a hospital-wide, observational cohort study. Intensive Care Med 2018;44(7):1017–26.
63. Singer P, Blaser AR, Berger MM, et al. ESPEN guideline on clinical nutrition in the intensive care unit. Clin Nutr 2019;38(1):48–79.
64. Vaschetto R, Pecere A, Perkins GD, et al. Effects of early extubation followed by noninvasive ventilation versus standard extubation on the duration of invasive mechanical ventilation in hypoxemic non-hypercapnic patients: a systematic review and individual patient data meta-analysis of randomized controlled trials. Crit Care 2021;25(1):189.
65. Osadnik CR, Tee VS, Carson-Chahhoud KV, et al. Non-invasive ventilation for the management of acute hypercapnic respiratory failure due to exacerbation of chronic obstructive pulmonary disease. Cochrane Database Syst Rev 2017;7(7):CD004104.
66. Xu XP, Zhang XC, Hu SL, et al. Noninvasive ventilation in acute hypoxemic non-hypercapnic respiratory failure: a systematic review and meta-analysis. Crit Care Med 2017;45(7):e727–33.

67. David-João PG, Guedes MH, Réa-Neto Á, et al. Noninvasive ventilation in acute hypoxemic respiratory failure: a systematic review and meta-analysis. J Crit Care 2019;49:84–91.
68. Ferreyro BL, Angriman F, Munshi L, et al. Association of noninvasive oxygenation strategies with all-cause mortality in adults with acute hypoxemic respiratory failure: a systematic review and meta-analysis. JAMA 2020;324(1):57–67.
69. Girard TD, Alhazzani W, Kress JP, et al. An official American Thoracic Society/American College of Chest Physicians clinical practice guideline: liberation from mechanical ventilation in critically ill adults. Rehabilitation protocols, ventilator liberation protocols, and cuff leak tests. Am J Respir Crit Care Med 2017;195(1):120–33.
70. Ouellette DR, Patel S, Girard TD, et al. Liberation from mechanical ventilation in critically ill adults: an official American college of chest physicians/American thoracic society clinical practice guideline: inspiratory pressure augmentation during spontaneous breathing trials, protocols minimizing sedation, and noninvasive ventilation immediately after extubation. Chest 2017;151(1):166–80.
71. Devlin JW, Skrobik Y, Gélinas C, et al. Executive summary: clinical practice guidelines for the prevention and management of pain, agitation/sedation, delirium, immobility, and sleep disruption in adult patients in the ICU. Crit Care Med 2018;46(9):1532–48.
72. Wang J, Ren D, Liu Y, et al. Effects of early mobilization on the prognosis of critically ill patients: a systematic review and meta-analysis. Int J Nurs Stud 2020;110:103708.
73. Zang K, Chen B, Wang M, et al. The effect of early mobilization in critically ill patients: a meta-analysis. Nurs Crit Care 2020;25(6):360–7.
74. Waldauf P, Jiroutková K, Krajčová A, et al. Effects of rehabilitation interventions on clinical outcomes in critically ill patients: systematic review and meta-analysis of randomized controlled trials. Crit Care Med 2020;48(7):1055–65.