# Pulmonary Emergencies

## Pneumonia, Acute Respiratory Distress Syndrome, Lung Abscess, and Empyema

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**KEYWORDS**

• Pneumonia • Acute respiratory distress syndrome • Lung abscess • Empyema
• Respiratory infections • Pulmonary emergencies

**KEY POINTS**

- Lower respiratory tract infections are a leading cause of death in the United States.
- Community-acquired and hospital-acquired pneumonia, acute respiratory distress syndrome, lung abscess, and empyema can present as life-threatening infections of the respiratory system.
- Early diagnostic and treatment strategies are required to effectively treat these infections and prevent complications.

### INTRODUCTION

Infections of the respiratory tract constitute a major source of morbidity and mortality in the United States. Lower respiratory tract infections are the third leading cause of death in the United States after ischemic heart disease and cerebrovascular disease, accounting for 6.6% of all deaths. Development of new antibiotics and vaccines has not been fully successful in eliminating the morbidity and mortality associated with respiratory infections. Antibiotic resistance among common respiratory pathogens has emerged in the last 2 to 3 decades. Community-acquired and hospital-acquired pneumonia, acute respiratory distress syndrome (ARDS), lung abscess, and empyema can present as life-threatening infections of the respiratory system, which require early diagnosis and treatment to prevent complications and mortality. This review discusses diagnostic and treatment interventions for these pulmonary emergencies.

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## PNEUMONIA

Severe community-acquired pneumonia (CAP), hospital-acquired/health care-associated pneumonia (HCAP), and ventilator-associated pneumonia (VAP) constitute a large percentage of respiratory tract infections requiring admission to an intensive care unit (ICU).

### *CAP*

CAP is defined as an acute infection of the lung parenchyma acquired outside hospitals or extended-care facilities and accompanied by symptoms of acute illness.[1] CAP remains a major health problem in the United States, with more than 60,000 deaths annually.[2] In adults, CAP results in approximately 600,000 hospital admissions annually and ranks as the eighth leading cause of death. Mortality from CAP varies dramatically depending on the severity of the illness and associated comorbidities. Mortality is less than 1% to 5% in the outpatient setting and it approaches 23% in hospitalized patients.[2] In more seriously ill patients with bacteremia who require ICU admission, mortality can approach more than 40%.[3,4]

#### *Pathophysiology*

The common mechanisms for the development of pneumonia are inhalation of microorganisms into the lower airways and aspiration of oropharyngeal contents. Other mechanisms include direct spread from a contiguous site and distant hematogenous spread from an extrapulmonary focus. *Streptococcus pneumoniae* is the most common pathogen isolated from patients with CAP.[5,6] The common pathogens responsible for CAP are listed in **Table 1**.[7] In addition to *Streptococcus pneumoniae*, other typical pathogens that account for CAP include *Haemophilus influenzae, Staphylococcus aureus,* group A *Streptococci, Moraxella catarrhalis,* anaerobes, and aerobic gram-negative bacteria. The classically described atypical pneumonia refers to pneumonia caused by *Legionella* species, *Mycoplasma pneumoniae*, *Chlamydophila pneumoniae*, and *Chlamydophila psittaci*. However, the term atypical should no longer be used. In recent years, community-acquired methicillin-resistant *Staphylococcus aureus* (MRSA) has emerged as an important pathogen responsible for severe, fulminant necrotizing pneumonia in young, healthy individuals without typical risk factors.[8,9]

**Table 1**
**Common pathogens in CAP by level of care**

| | |
|---|---|
| Outpatients | *Streptococcus pneumoniae, Mycoplasma pneumoniae, Haemophilus influenzae, Chlamydophila pneumoniae,* respiratory viruses (influenza A and B, adenovirus, respiratory syncytial virus, parainfluenza) |
| Inpatients (non-ICU) | *Streptococcus pneumoniae, Mycoplasma pneumoniae, , Chlamydophila pneumoniae, Haemophilus influenzae, Legionella* spp, respiratory viruses |
| Inpatients (ICU) | *Streptococcus pneumoniae, Legionella* spp, *Haemophilus influenzae,* gram-negative bacilli, *Staphylococcus aureus* |

*Data from* Leroy O, Santre C, Beuscart C, et al. A five-year study of severe community-acquired pneumonia with emphasis on prognosis in patients admitted to an intensive care unit. Intensive Care Med 1995;21(1):24–31.

### *Clinical evaluation*

Common clinical features of CAP include cough, fever, sputum production, and pleuritic chest pain. Patients may have gastrointestinal symptoms such as nausea, vomiting, or diarrhea. Other symptoms may include fatigue, headache, myalgia, and arthralgia. Risk stratification is an important component in the management of a patient with CAP and various risk stratification indices have been used to determine appropriate care setting (outpatient, inpatient non-ICU, ICU). Various prediction scores including the Pneumonia Severity Index (PSI), CURB 65 (confusion, urea >19 mg/dL; respiratory rate >30; low blood pressure: systolic <90 mm Hg or diastolic <60 mm Hg; and age >65 years), and CRB 65 (confusion, respiratory rate >30; low blood pressure: systolic <90 mm Hg or diastolic <60 mm Hg; and age >65 years) have been shown to reliably predict mortality in patients with CAP.[10–12] CRB 65 is simple to calculate and is based solely on physical examination findings and does not require laboratory data. The indications for ICU admission besides patients in need for mechanical ventilation and those in septic shock are listed in **Box 1**.[7]

### *Diagnosis*

Although it is thought that pathogen-directed therapy is better than empiric therapy, a randomized trial failed to show such benefit.[13] Routine diagnostic tests are optional for outpatient treatment of CAP. Patients with severe CAP requiring ICU admission should have

- Blood cultures
- Urinary antigen tests for *Legionella pneumophila* and *Streptococcus pneumoniae*
- Expectorated sputum for Gram stain and culture

**Box 1**
**Criteria for ICU admission in CAP**

*Major Criteria*

- Requirement for mechanical ventilation
- Septic shock (SBP <90 mm Hg despite fluids)

*Minor Criteria (3 or more)*

- White blood cell count >30 $\times$ $10^9$/L or <4 $\times$ $10^9$/L
- Blood urea nitrogen >20 mg/dL
- $Pao_2$ (partial pressure of oxygen, arterial )/$F_{IO_2}$ (fraction of inspired oxygen) <250
- Multilobe involvement
- Respiratory rate >30/min
- Platelet count <100,000 $\times$ $10^9$/L
- Confusion/disorientation
- Hypothermia (temperature <36°C)
- Hypotension requiring fluid resuscitation

*Modified from* Mandell LA, Wunderink RG, Anzueto A, et al. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. Clin Infect Dis 2007;44(Suppl 2):S27–72.

- Intubated patients require endotracheal aspirate (ETA) (fresh) or m-BAL (blind bronchoalveolar lavage)
- Nasopharyngeal swab for influenza during seasonal influenza (rapid antigen test and viral polymerase chain reaction)

Even with extensive diagnostic evaluation, the cause is not identified in as many as 50% of patients.[5,6,14,15]

***Treatment***

Antimicrobial agents are the cornerstone of treatment in patients with CAP. Antibiotic therapy is typically begun on an empiric basis. Macrolides, quinolones, and second-generation/third-generation cephalosporins are considered the antimicrobial agents of choice for patients with CAP. However, resistance to antibiotics has been an increasingly recognized problem in the therapy for CAP. Risk factors for drug-resistant *Streptococcus pneumoniae* in adults include:

- Age >65 years
- β-lactam, macrolide, or fluoroquinolone therapy within the past 3 to 6 months
- Alcoholism
- Medical comorbidities
- Immunosuppressive illness or therapy
- Exposure to a child in a day care center

Two retrospective analyses of large Medicare databases identified that the time between presentation to the hospital and the time to the first antibiotic dose is a predictor of patient outcome when patients require hospital admission.[16,17] The antibiotic regimens advocated by a collaboration between the Infectious Disease Society of America and the American Thoracic Society (IDSA/ATS) in 2007 are summarized in **Figs. 1** and **2**.[7] The antibiotic therapy should be continued for a minimum of 5 days,

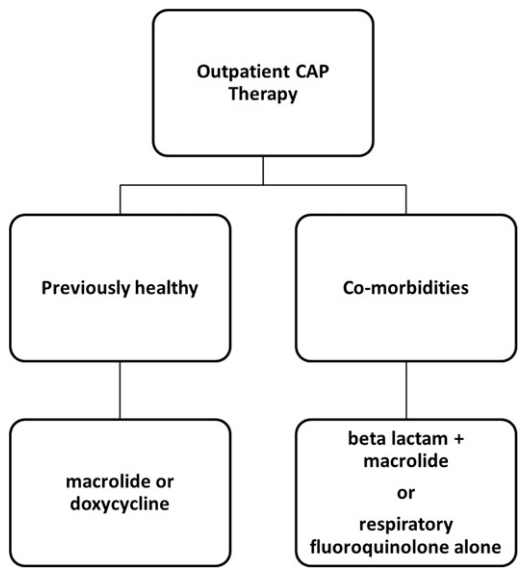


**Fig. 1.** ATS/IDSA guidelines for outpatient CAP treatment. (*Data from* Mandell LA, Wunderink RG, Anzueto A, et al. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. Clin Infect Dis 2007;44(Suppl 2):S29.)

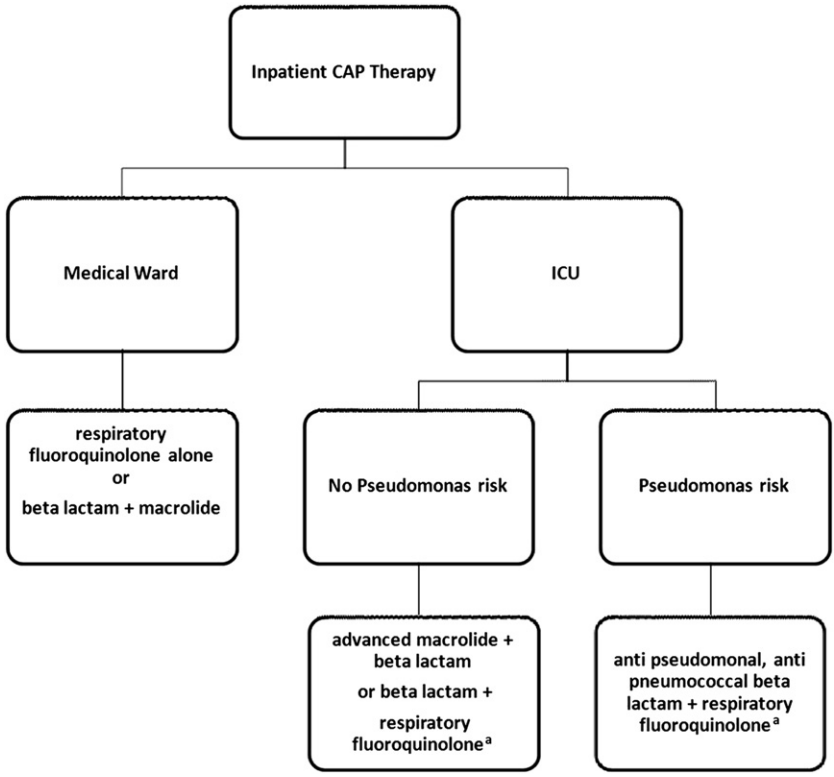


**Fig. 2.** ATS/IDSA guidelines for inpatient CAP treatment. [a] Add vancomycin or linezolid for suspected community-acquired MRSA infection. (*Data from* Mandell LA, Wunderink RG, Anzueto A, et al. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. Clin Infect Dis 2007;44(Suppl 2):S30.)

except for azithromycin, which has a long half-life and for which a shorter duration might be adequate. Longer duration of therapy may be needed in patients with necrotizing pneumonia, lung abscess, or empyema; those with associated extrapulmonary infections; pneumonia caused by *Pseudomonas aeruginosa* or *Legionella* species; and those with inappropriate initial empiric therapy.

### *HCAP*

HCAP refers to patients with pneumonia who had recent hospitalization in the last 90 days, had residence in a nursing home or extended-care facility, were receiving chronic hemodialysis, were receiving home wound care, or had exposure to a family member with a drug-resistant pathogen infection.[18] HCAP is the second most common health care-related infection after urinary tract infection. HCAP accounts for 17% to 18% of pneumonia requiring hospitalization.[19,20]

#### *Pathophysiology*

The pathogenesis of HCAP includes a combination of immune impairment caused by underlying comorbidities, acquisition of a resistant strain, and exposure to large inocula of bacteria. Colonization of the upper respiratory tract followed by aspiration

of bacteria-laden oropharyngeal secretions in to the lower respiratory tract is the most likely mechanism for development of HCAP. Common pathogens responsible for HCAP are listed in **Box 2**.[19–21]

***Clinical evaluation***

The clinical presentation of patients with HCAP is similar to patients with CAP. However, elderly patients and patients residing in long-term care (LTC) facilities might not have classic signs of infection. Compared to patients with CAP, these patients are less likely to have a productive cough, chills, myalgia, or arthralgia.[22] Patients from LTC facilities are more likely to present with altered mental status, tachypnea, and hypotension.[23] These atypical findings could be responsible for a delay in diagnosis and treatment, contributing to increased morbidity and mortality in this group of patients.

***Diagnosis***

There is no established gold standard for the diagnosis of HCAP. Fever, purulent cough, and new infiltrate on chest radiograph are considered to be the mainstay of diagnosis of pneumonia. In contrast to CAP, the value of sputum Gram stain in non-intubated patients with HCAP is questionable because of higher rates of oropharyngeal colonization in recently hospitalized patients or older patients residing in LTC facilities.[24,25] Transtracheal aspiration and bronchial washings are more accurate means of obtaining specimens for Gram stain and culture. Blood cultures and urinary antigen detection can be helpful in identifying the cause.

***Treatment***

Patients with HCAP are at higher risk of receiving inadequate antimicrobial therapy compared with CAP and are more likely to have a worse outcome.[19] Lack of adequate coverage for multidrug-resistant (MDR) pathogens is considered to be a contributing factor for this discrepancy between HCAP and CAP outcomes. Risk factors for isolation of MDR pathogens include severely ill patients requiring ICU admission, low functional status, and exposure to antibiotics for more than 3 days in previous 6 months.[26] The approach to initial empiric antimicrobial treatment of HCAP is summarized in **Fig. 3**.[27]

**Box 2**
**Common pathogens for HCAP**

*Gram-Positive Bacteria*

*Staphylococcus aureus*

*Streptococcus pneumoniae*

MRSA

*Gram-Negative Bacteria:*

*Pseudomonas aeruginosa*

*Klebsiella pneumoniae*

*Escherichia coli*

*Haemophilus influenza*

*Data from* Refs.[19–21]

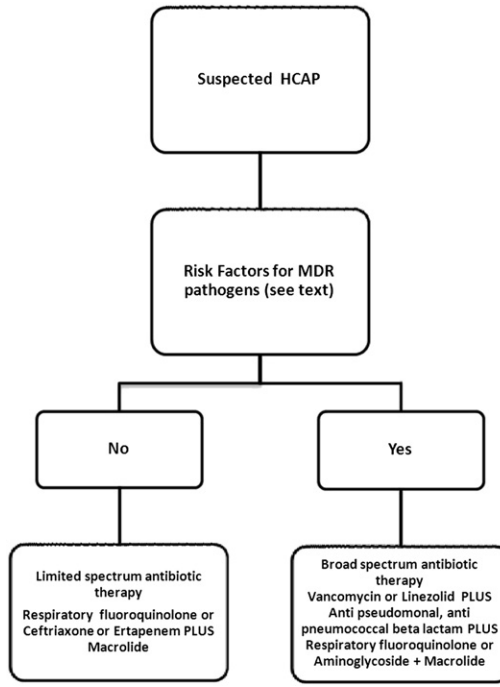


**Fig. 3.** Initial empiric antimicrobial therapy for HCAP. (*Data from* El-Solh AA. Health care-associated pneumonia. In: Sethi S, editor. Respiratory infections. 1st edition. New York: Informa Healthcare; 2010. p. 114–25.)

## *VAP*

VAP is defined as a pneumonia that develops after 48 hours of mechanical ventilation. Pathogens causing late-onset VAP ($\geq$5 days) are more likely to have MDR compared to those responsible for early-onset VAP (<5 days). VAP is the commonest nosocomial infection in the ICU, leading to increased morbidity, mortality, and health care costs.[18,28] VAP complicates the hospital course of about 20% of patients receiving mechanical ventilation. Rates of VAP increase with the duration of mechanical ventilation, with attack rates estimated to be approximately 3% per day.[18,28]

### *Pathophysiology*

VAP pathogenesis begins with bacterial colonization that may progress to ventilator-associated tracheobronchitis and in some patients to VAP. In mechanically ventilated patients, colonization of the oropharynx with potentially pathogenic organisms occurs within 36 hours of intubation. Leakage of bacteria around the endotracheal tube cuff is a major route of access to the lower respiratory tract and a target for VAP prevention efforts. The common pathogens causing VAP are listed in **Table 2**. VAP caused by MDR organisms is associated with increased mortality. The risk factors for VAP caused by MDR organisms are listed in **Box 3**.

### *Clinical evaluation*

The clinical criteria that have traditionally been used to diagnose VAP include a new or progressive pulmonary infiltrate, fever, leukocytosis, and increase in tracheobronchial

**Table 2**
**Pathogens in VAP**

| Common Pathogens | Less Common Pathogens |
|---|---|
| *Pseudomonas aeruginosa* | *Escherichia coli* |
| MRSA | *Enterobacter* spp |
| *Klebsiella pneumoniae* | *Citrobacter* spp |
| *Acinetobacter* spp | *Serratia* spp |
| *Stenotrophomonas maltophilia* | *Legionella* spp |
| *Streptococcus pneumoniae* (early VAP) | |
| *Haemophilus influenzae* (early VAP) | |

secretions. However, these clinical criteria are nonspecific and of little clinical usefulness in the diagnosis of VAP.[29,30] The Clinical Pulmonary Infection Score (CPIS) was developed as a noninvasive method to diagnose VAP[31] and uses a combination of clinical features together with the culture of a tracheal aspirate to diagnose pneumonia. The CPIS assigns 0 to 12 points based on 6 clinical criteria:

- Fever
- Leukocyte count
- Oxygenation
- Quantity and purulence of secretions
- Type of radiographic abnormality
- Results of respiratory (tracheal aspirate) Gram stain and culture

***Diagnosis***

Because the clinical criteria of VAP lack specificity, several diagnostic techniques have been reported that attempt to distinguish patients with lung infection from those colonized with potentially pathogenic organisms or those with tracheobronchitis. ETA, BAL, and protective specimen brush (PSB) have been used to detect pathogenic bacteria in the lower respiratory tract. Studies have shown conflicting results in outcomes when noninvasive and invasive techniques to collect lower respiratory tract samples were compared.[32,33] Biological markers, such as procalcitonin, C-reactive protein, and soluble triggering receptor expressed on myeloid cells, may be helpful adjuncts for the diagnosis and management of VAP.[34]

**Box 3**
**Risk factors for infection by MDR organisms**

- Intubation for longer than 7 days
- Previous broad-spectrum antibiotics
- Hemodialysis
- Hospitalization for 2 days or more in the last 90 days
- Previous admission to the ICU
- Nursing home residence
- Immunosuppression
- Chronic wound care

### *Treatment*

The most important factor determining the outcome of VAP is the early initiation of appropriate antibiotic therapy. Because of the spectrum of potential pathogens and the increasing prevalence of MDR organisms, a broad-spectrum, multidrug, empiric antibiotic protocol is required in most patients with suspected VAP (except those at low risk of infection with an MDR organism). BAL and quantitative culture allows for the de-escalation of antibiotics once a pathogen(s) is identified. Initial empiric antimicrobial therapies for early-onset and late-onset VAP are summarized in **Tables 3** and **4**.[18] Antibiotic therapy should be modified based on the identification and drug resistance of pathogens. Antimicrobial therapy is recommended for 7 to 8 days for uncomplicated VAP except when VAP is caused by *Pseudomonas aeruginosa* when antimicrobial therapy should be continued for longer duration (10–14 days).[18,35]

## ARDS

ARDS is an important cause of ICU admission and is associated with high mortality.[36] ARDS is an acute, diffuse, inflammatory lung injury that is characterized by hypoxemia ($Pa_{O_2}/Fi_{O_2}$ <200), bilateral radiographic opacities, and no evidence of increased left atrial pressure. The common conditions associated with ARDS are listed in **Box 4**. Sepsis (both from pulmonary and extrapulmonary causes) is a leading cause of ARDS. Lung infection may account for 50% of cases of ARDS.[37,38] Superinfection with bacterial pathogen is also possible with ARDS from other causes because of impaired host defenses and prolonged mechanical ventilation.[39] Pneumonia can be a cause or complication of ARDS. The diagnosis of pulmonary infection in patients with ARDS is often difficult. The incidence of VAP during ARDS varied from 15% to 60% in different studies.[38,40–43]

### *Pathophysiology*

CAP is a common cause for ARDS that develops outside the hospital.[44] Common pathogens include *Streptococcus pneumoniae*, *Legionella pneumophila*, *Pneumocystis jirovecii*, *Staphylococcus aureus*, enteric gram-negative organisms, and respiratory viruses.[6] Common pathogens responsible for pneumonia in patients with ARDS

**Table 3**
**Initial empiric antimicrobial therapy for early-onset VAP**

| HAP/VAP, Early-Onset (ie, No Risk Factors for MDR Pathogens), Any Disease Severity | |
|---|---|
| **Potential Pathogen** | **Recommended Antibiotic** |
| *Streptococcus pneumoniae*<br>*Haemophilus influenzae*<br>Methicillin-sensitive *Staphylococcus aureus* (MSSA)<br>Antibiotic-sensitive enteric gram-negative bacilli:<br>• *Escherichia coli*<br>• *Klebsiella pneumoniae*<br>• *Enterobacter* spp<br>• *Proteus* spp<br>• *Serratia marcescens* | Ceftriaxone<br>or<br>ciprofloxacin, levofloxacin or moxifloxacin<br>or<br>ampicillin/sulbactam<br>or<br>ertapenem |

*Data from* American Thoracic Society, Infectious Diseases Society of America. Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. Am J Respir Crit Care Med 2005;171(4):388–416.

**Table 4**
**Initial empiric antimicrobial therapy for late-onset VAP**

| HAP/VAP/HCAP, Late-Onset (ie, Risk Factors for MDR pathogens), Any Disease Severity | |
|---|---|
| **Potential Pathogen** | **Combination Antibiotic Therapy** |
| *Streptococcus pneumoniae*<br>*Haemophilus influenzae*<br>*Staphylococcus aureus*<br>Antibiotic-sensitive enteric gram-negative bacilli:<br>• *Escherichia coli*<br>• *Klebsiella pneumoniae*<br>• *Enterobacter* spp<br>• *Proteus* spp<br>• *Serratia marcescens*<br>MDR Pathogens:<br>• *Pseudomonas aeruginosa*<br>• *Klebsiella pneumoniae* (ESBL+)<br>• *Acinetobacter* spp<br>• MRSA<br>• *Legionella pneumophila* | Antipseudomonal cephalosporin (cefepime, ceftazidime)<br>or<br>antipseudomonal carbepenem (imipenem or meropenem)<br>or<br>β-lactam/β-lactamase inhibitor (piperacillin-tazobactam)<br>plus<br>antipseudomonal fluoroquinolone (ciprofloxacin or levofloxacin)<br>or<br>aminoglycoside (amikacin, gentamicin, or tobramycin)<br>plus<br>linezolid or vancomycin |

*Data from* American Thoracic Society, Infectious Diseases Society of America. Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. Am J Respir Crit Care Med 2005;171(4):388–416.

include MRSA, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, *Stenotrophomonas maltophili*, and *Enterobacteriaceae.*[38,40] Effects of mechanical ventilation on bacterial growth, on lung inflammation, and on systemic inflammation have been believed to play a role in the pathogenesis of pneumonia during ARDS. Impaired

**Box 4**
**Common conditions associated with ARDS**

- Sepsis
- Aspiration
- Pneumonia
- Severe trauma
- Burns
- Multiple blood transfusions
- Pancreatitis
- Drug overdose
- Near drowning
- Smoke inhalation
- Cardiopulmonary bypass
- Pulmonary contusion
- Multiple fractures
- Venous air embolism
- Amniotic fluid embolism
- Neurogenic pulmonary edema

host defenses during ARDS and mechanical ventilation increase host susceptibility to infection with virulent or resistant organisms.

### *Clinical Evaluation*

Initial clinical presentation is that of the underlying condition responsible for ARDS. Clinical symptoms of ARDS become apparent after 48 to 72 hours of inciting event. Dyspnea, tachypnea, hypoxia, and cough are generally present. Persistent or new fever, purulent respiratory secretions, oxygenation desaturation, tachycardia, hemodynamic instability or septic shock suggest VAP in mechanically ventilated patients with ARDS. The CPIS[31] can be helpful to diagnose new VAP in patients with ARDS.

### *Diagnosis*

Diagnosis of new respiratory infection in patients with ARDS who are on mechanical ventilation is challenging. Physicians should have a low threshold for invasive procedures to diagnose new respiratory infections, because many of these patients have an abnormal chest radiograph with infiltrates, hypoxia, and fever at the time of initial presentation. Respiratory tract cultures can be obtained with ETA, BAL, PSB, or plugged telescopic catheter (PTC). Quantitative cultures of these samples help distinguish colonization from true pulmonary infection (**Table 5**).[45] Efforts should be made to obtain bacteriologic samples before initiating or modifying antibiotic treatment.

### *Treatment*

General goals of treatment of ARDS include treatment of underlying condition, lung protective mechanical ventilation, sedation, nutritional support, deep vein thrombosis and stress ulcer prophylaxis, and measures to avoid nosocomial infections. Principles of antimicrobial treatment of VAP during ARDS are similar to treatment of late-onset VAP, because infection with MDR pathogens is more likely in these patients. **Box 5** summarizes strategies for preventing VAP.

## LUNG ABSCESS

Lung abscess is defined as necrosis of lung parenchyma as a result of microbial infection. Lung abscesses were more common in the preantibiotic era as a result of the complication of bacterial pneumonia. The incidence and mortality of lung abscess have decreased significantly over the last few decades. In the postantibiotic era, most lung abscesses arise as a complication of aspiration pneumonia.[50] Lung abscesses can be classified as acute (<1 month of symptoms) or chronic (>1 month of symptoms), based on the causative organism (eg, pneumococcal lung abscess, anaerobic lung abscess) or on the underlying conditions. When an abscess develops

**Table 5**
**Microbiological culture thresholds for the diagnosis of VAP**

| Sampling Technique | Quantitative Culture Threshold (cfu/mL) |
|---|---|
| ETA | $10^6$ |
| BAL | $10^4$ |
| PSB | $10^3$ |
| PTC | $10^3$ |

*Modified from* Richard Jean-Damien DD, Roux D. Pneumonia in ARDS. In: Sethi S, editor. Respiratory Infections. New York: Informa Healthcare; 2009. p. 153.

**Box 5**
**Strategies for preventing VAP**

- Semirecumbent position with head elevation up to 30° to 45°[46]
- Oral care with chlorhexidine[47]
- Implement weaning and wake-up protocols
- Limited use of proton pump inhibitors and sucralfate[38,48]
- Avoid gastric overdistention
- Early tracheotomy[49]

in individuals prone to aspiration or individuals in relatively good health, it is termed primary lung abscess. Secondary lung abscess implies underlying predisposing conditions like malignant neoplasm, complications of surgery, and immunosuppression. Approximately 80% of lung abscesses are primary.[51]

### *Pathophysiology*

Anaerobic bacteria generally present in gingival crevices are responsible for aspiration pneumonia and lung abscess.[52] Primary lung abscess is rare in an edentulous person. Risk factors for aspiration pneumonia and lung abscess include reduced level of consciousness, periodontal disease, esophageal dysmotility, gastric reflux, dysphagia, vomiting, gastric overdistension, large-volume tube feedings, and recumbent position. After the initial inoculum of bacteria with large-volume aspiration, pneumonitis develops followed by tissue necrosis in 7 to 14 days depending on the host-pathogen interaction. This tissue necrosis results in lung abscess. Other mechanisms of development of lung abscess include septic embolization from right-sided infective endocarditis and hematogenous spread from suppurative thrombophlebitis. Lung abscesses from septic embolization are generally multiple, and involve noncontiguous areas of the lung. Both anaerobic and aerobic bacteria are known to cause lung abscess, with anaerobes being more common (**Box 6**). Anaerobic lung abscesses are typically polymicrobial. *Nocardia* is also known to cause lung abscesses in immunocompromised patients.

**Box 6**
**Common pathogens for lung abscess**

- *Peptostreptococcus*
- *Prevotella*
- *Bacteroides*
- *Fusobacterium*
- *Streptococcus milleri*
- *Streptococcus pyogenes*
- *Staphylococcus aureus*
- *Klebsiellae pneumoniae*
- *Escherichia coli*
- *Pseudomonas aeruginosa*

Certain parasites (*Entamoeba histolytica* and *Paragonimus westermani*) and fungi (*Aspergillus, Blastomyces,* and *Histoplasma*) can cause lung abscesses.

### *Clinical Evaluation*

Primary lung abscess caused by anaerobic bacteria usually presents in a subacute fashion with symptoms for several weeks.[50,53] Cough, fever, and purulent sputum are common presenting symptoms of lung abscess. The sputum has a putrid smell in about 50% of cases. Patients may present with pleuritic chest pain, hemoptysis, weight loss, or night sweats. Physical examination findings include fever, poor dentition and gingival disease, and amphoric or cavernous breath sounds on auscultation. Clubbing of the fingers and absent gag reflex may also be present. Associated empyema is present in about one-third of cases and may be seen with or without bronchopleural fistula. Necrotizing pneumonia caused by *Staphylococcus aureus* or *Klebsiella pneumoniae* occasionally presents with a more rapid course, high-grade fever, marked leukocytosis, and early extension to pleural space.

### *Diagnosis*

Lung abscess is usually diagnosed by chest radiograph showing a thick-walled cavity with air fluid level. However, computed tomography (CT) is more sensitive than chest radiography and is useful to detect small cavities, to identify associated malignancy, and to distinguish lung abscesses from empyema.[54] Multilobar involvement suggests secondary lung abscess and impaired host defenses.[55] It is difficult to isolate anaerobic bacteria in primary lung abscess because most respiratory tract specimens are contaminated by upper airway flora and are consequently inappropriate for anaerobic culture. As a result, treatment of anaerobic infection can be started without microbiological studies, with a classic presentation of subacute illness in a typical aspiration-prone patient with gingival disease and foul-smelling sputum with putrid odor.[51] Uncontaminated specimens can be obtained by transtracheal aspirates (TTA), transthoracic needle aspirates (TTNA), pleural fluid, or blood cultures.[56,57] The usefulness of BAL or PSB for diagnosis of lung abscess is not well established. Blood cultures are rarely positive in anaerobic lung abscess. TTA and TTNA are not routinely performed to confirm the diagnosis. Patients without the classic presentation and with secondary lung abscess should have expectorated sputum checked for aerobic bacteria, mycobacteria, fungi, and, in some instances, parasites. Bronchoscopy is indicated to detect underlying lesions in patients with atypical presentations and for those who fail standard therapy.

### *Treatment*

#### *Antibiotics*

Patients with large abscesses and excessive coughing should be placed in a lateral decubitus position with the abscess side down to avoid sudden discharge of abscess contents causing asphyxiation or spread of infection to healthy lung segments. Standard treatment of primary lung abscess is clindamycin 600 mg intravenously every 8 hours initially, followed by 150 to 300 mg orally 4 times daily. Penicillin was considered to be the drug of choice for primary lung abscess for many years but recent studies have shown superiority of clindamycin over penicillin in time to defervescence, time to resolution of putrid sputum, and relapse rates.[58,59] Monotherapy with metronidazole is not very effective,[60] but combination of penicillin and metronidazole has yielded favorable results and is inexpensive. Other agents that could be used in the treatment of lung abscess include combinations of a penicillin with a β-lactamase inhibitor, carbapenems, and quinolones with good anaerobic activity (moxifloxacin

and gatifloxacin).[61] Lung abscess caused by organisms other than anaerobes is best treated with antibiotics that are active against the infecting pathogen and penetrate the lung parenchyma. The preferred agents for MRSA are vancomycin and linezolid. The duration of antibiotic therapy is controversial. Patients are often treated for 6 to 8 weeks or more. One study using clindamycin to treat anaerobic lung abscess showed excellent efficacy with no advantage of 6 weeks over 3 weeks of therapy.[58] Some experts recommend continuing antibiotic treatment until the chest radiograph shows a small, stable residual lesion or is clear.

#### *Bronchoscopic drainage*

Studies in the preantibiotic era showed no advantage for bronchoscopic or postural drainage of abscesses compared with conservative management or surgery. Drainage of large abscesses may result in rapid unloading of the pus and necrotic material from the abscess into other lung segments and may produce acute asphyxiation or ARDS.[51] Bronchoscopy should be reserved for patients who fail standard therapy or patients with suspected endobronchial tumor.

#### *Surgery*

Lung abscesses, in contrast to other visceral abscesses, usually drain themselves, through communication with large airways. This drainage is indicated by the presence of air fluid levels. Almost all patients with lung abscess respond to appropriate antimicrobial therapy, and surgery (lobectomy or pneumonectomy) is reserved for the 10% to 15% of patients who do not improve with appropriate medical management. Causes of medical treatment failure include large cavities (>8 cm), abscesses caused by resistant organisms such as *Pseudomonas aeruginosa,* obstructing neoplasm, and massive hemoptysis. Percutaneous and endoscopic drainage can be tried in patients with poor surgical risk who fail medical treatment. Percutaneous procedures require special care to prevent contamination of the pleural space. Endoscopic drainage is performed by placing a pigtail catheter into the abscess cavity under bronchoscopic visualization, leaving the catheter in place until the cavity has drained.[62]

## EMPYEMA

Empyema is characterized by aspiration of pus from pleural space or positive Gram stain on pleural fluid analysis. Infections of the pleural space most commonly follow pneumonia, accounting for 40% to 60% of all empyemas. Thoracotomy is the next most common precursor of empyema, accounting for 20%, and trauma accounts for 4% to 10%. Common causes of empyema are shown in **Table 6**.[63–66]

#### *Pathophysiology*

Pleural effusions develop because of increased hydrostatic pressure or decreased oncotic pressure caused by cardiac, renal, hepatic, or metabolic diseases or because of altered pleural permeability caused by noninfectious inflammatory disease, infection, toxic injury, malignancy, or trauma. Pleural effusions are nutritionally rich media in which phagocytic defenses are severely impaired. The formation of an empyema has been arbitrarily divided into an exudative phase, during which pus accumulates; a fibropurulent phase, during which fibrin deposition and loculation of pleural exudate occurs; and an organization phase, during which fibroblast proliferation and scar formation cause lung entrapment. However, if pneumonia associated with a parapneumonic effusion is treated promptly with an appropriate antimicrobial agent, the cellular and cytokine mediators of inflammation are aborted. Resolution of uncomplicated parapneumonic effusions leaves the pleura essentially normal without clinically significant

**Table 6**
**Common causes of empyema**

| Cause | Percentage |
|---|---|
| Pulmonary infection (pneumonia) | 56 |
| Surgery (thoracotomy) | 22 |
| Trauma | 4 |
| Esophageal perforation | 4 |
| Complication of thoracentesis/chest tube | 4 |
| Subdiaphragmatic infection | 3 |
| Spontaneous pneumothorax | 1 |
| Septicemia | 1 |
| Other causes | 5 |

*Modified from* Bryant RE, Salmon CJ. Pleural empyema. Clin Infect Dis 1996;22(5):749.

fibrosis.[67] In the preantibiotic era, *Streptococcus pneumoniae* accounted for 60% to 70% of cases, *Streptococcus pyogenes* for 10% to 15% of cases, and *Staphylococcus aureus* for 5% to 10% of cases of empyema. *Streptococcus pneumoniae* now accounts for only 5% to 10% of cases, and many infections are mixed, with anaerobes present in 25% to 76% of empyemas either as sole organisms or in combination with other aerobic or facultative organisms.[68] Bacterial pathogens associated with nontuberculous pleural empyema are summarized in **Box 7**. Factors predisposing to aspiration such as altered mental status, alcoholism, and periodontal disease are common in patients with anaerobic infections of the pleura. Empyema complicating

**Box 7**
**Common pathogens for nontuberculous pleural empyema**

*Anaerobic Bacteria:*

*Bacteroides fragilis* group

*Prevotella* spp

*Fusobacterium nucleatum*

*Peptostreptococcus*

Microaerophilic streptococci

*Aerobic Bacteria:*

*Streptococcus pneumoniae*

*Streptococcus pyogenes*

*Streptococcus milleri*

*Staphylococcus aureus*

*Enterobacteriaceae*

*Klebsiella pneumoniae*

*Pseudomonas aeruginosa*

MRSA

hemothorax is often caused by *Staphylococcus*, whereas that associated with pneumothorax or hematogenous seeding of a serous effusion is often caused by aerobic gram-negative bacilli.[69] Immunocompromised patients are prone to pleural involvement with fungal, mycobacterial, or aerobic gram-negative bacillary infection.[65,70] Amoebic liver abscess is associated with pleural involvement in up to 15% to 20% of cases. Nocardia infections occur more frequently in patients with underlying conditions, such as organ transplantation, malignancy, diabetes mellitus, AIDS, and long-term use of steroids. Empyema caused by *Mycobacterium tuberculosis* is a rare disease in which pus is present in the pleural space and the predominant pleural cell is the polymorphonuclear leukocyte. Tuberculous empyema should be differentiated from tuberculous pleurisy, in which a lymphocytic effusion occurs from the immunologic response to tuberculous proteins.

### *Clinical Evaluation*

Patients with bacterial pneumonia usually present with fever, shortness of breath, productive cough, and chest pain. Patients with anaerobic pleuropulmonary infection present with an indolent course and may show weight loss, fever, and chronic cough. A history of aspiration is often obtained and poor oral hygiene is often evident. The presence of persistent fever, chest pain, or leukocytosis despite the administration of appropriate antibiotics should suggest the presence of an empyema in patients with pulmonary or adjacent infection. Physical examination is remarkably nonspecific and reveals decreased breath sounds, dullness to percussion, and crackles over the affected area. Chronic empyemas may erode the chest wall and present with a spontaneous draining abscess, termed empyema necessitatis.[68]

### *Diagnosis*

Chest radiograph and ultrasonography play an important role in the evaluation of empyema. As little as 25 mL of pleural fluid can elevate the hemidiaphragm radiographically, but blunting of the posterior costophrenic sulcus usually requires about 200 mL of fluid. The lateral decubitus chest film can detect as little as 5 mL of free pleural fluid.[71] Ultrasonography is particularly useful for detecting small amounts of pleural fluid, for easy identification of free or loculated pleural effusions, and for differentiating loculated effusions from solid masses. Ultrasonography also helps in diagnostic thoracentesis and pleural drainage. A chest CT scan with intravenous contrast is sometimes required for optimal evaluation of an empyema or loculated effusion. Thickening of the parietal pleura is suggestive of empyema.

An effusion should be sampled if the fluid is free flowing, is greater than 10 mm on a lateral decubitus film, or is loculated. Empyema fluid might appear purulent, bloody, or cloudy, with a very high white blood cell count (>50,000). Empyema fluid characteristically has a pH of less than 7.2, a glucose level of less than 40 mg/dL, and lactate dehydrogenase activity of at least 1000 IU/L.[72] Malodorous empyema fluid suggests the presence of anaerobic infection but is present in only about two-thirds of anaerobic empyemas. Most experts recommend drainage of the pleural space for a positive pleural fluid culture or Gram stain. However, only 61% of patients with established empyemas have a positive Gram stain. Although most patients with empyemas have a positive culture, the absence of growth does not mean that a pleural effusion does not require drainage.[73] A pleural fluid pH less than 7.2 indicates the need for drainage.[74] Spurious increase of empyema fluid pH values may occur in patients with urea-splitting *Proteus* infections.[75] The diagnosis of amoebic abscess with subdiaphragmatic rupture is suggested by the anchovy paste or chocolate appearance of pleural fluid. Approximately 98% of patients with pleural or pulmonary amebiasis have

positive serologic tests for *Entamoeba histolytica.* Patients at risk of fungal empyema require appropriate smears and cultures of empyema fluid for detection of fungi. For patients at risk of nocardial infection of the lung and pleura, modified acid-fast stains of purulent secretions should be performed. Pleural tuberculosis can be confirmed by acid-fast smears of pleural fluid in fewer than one-quarter of cases but can be diagnosed by pleural biopsy and culture in more than 90% of patients.[76]

### *Treatment*

#### *Antibiotics*

Effective therapy for an empyema requires control of infection, drainage of pus, and expansion of the lung. Initial empiric antimicrobial therapy should be based on the most likely pathogens, local antimicrobial susceptibility patterns, and all available results, including Gram stains. Most of the antibiotics adequately penetrate the pleural space except for aminoglycosides, which may be inactivated at low pleural fluid pH. Choices for initial empiric antibiotic therapy include a combination of a β-lactam and a β-lactamase inhibitor (amoxicillin/clavulanate, ampicillin/sulbactam, or piperacillin/tazobactam), a carbapenem (imipenem, ertapenem, or meropenem), or combination therapy with a third-generation cephalosporin (cefotaxime, ceftriaxone, or cefepime) and either clindamycin or metronidazole. These choices cover the most common pathogens associated with pleural empyema, including anaerobic organisms. Vancomycin should be added when infection with *Staphylococcus aureus* is suspected. The duration of antibiotic therapy for bacterial empyema depends on the sensitivity of the organism(s), response to initial therapy, extent of pulmonary parenchymal and pleural disease, adequacy of drainage, and host factors such as immune status. Prolonged antimicrobial therapy (4–6 weeks) may be necessary. Patients with pulmonary actinomycosis or nocardiosis may require 6 to 12 months of antimicrobial treatment.[77] Patients with tuberculous pleural disease should be treated with the same regimen and for the same duration as those with pulmonary tuberculosis. Patients infected with *Candida* species should receive an appropriate antifungal drug (fluconazole, caspofungin, or amphotericin B) for 2 weeks after the resolution of signs and symptoms of infection.[78] Amoebic empyema should be treated with pleural drainage and an appropriate antimicrobial agent. Metronidazole is considered the drug of choice and is administered for 10 days.

#### *Drainage of empyema*

In addition to antimicrobial therapy to control infection, drainage of pus is a major component of adequate treatment of pleural empyema. Repeated thoracentesis is rarely successful in such cases. Options for pleural drainage include tube thoracostomy, video-assisted thoracoscopic surgery (VATS), open decortication, and open thoracostomy. Tube thoracostomy (also known as chest tube) drainage is the least invasive option for drainage of empyema fluid. It is generally preferred over more invasive options for patients with uniloculated effusions and free-flowing fluid, but is also frequently used to drain multiloculated empyemas. Chest tubes are typically left in place until the drainage rate has decreased less than 50 mL/d and the empyema cavity has closed. Closed chest tube drainage without fibrinolytic therapy is successful in up to two-thirds of patients.[79] The most common reason for closed chest tube failure is pleural adhesions and intrapleural loculations that do not communicate with the chest tubes. When patients do not respond to chest tube drainage, a more definitive approach is needed.

Intrapleural administration of fibrinolytic agents (streptokinase, urokinase, and tissue plasminogen activator [TPA]) has been studied as a way to improve drainage

of loculated parapneumonic effusions and empyemas. However, data are conflicting regarding the benefit of this approach.[80–83] A Cochrane review failed to show a reduction in death among patients who received fibrinolytic therapy. When surgical intervention was included as an end point, fibrinolytics reduced the risk of this specific outcome.[84] In a recent study, concomitant use of intrapleural DNase and TPA resulted in a greater decrease in radiographic pleural opacity, a lower rate of surgical referral, and a shorter hospital stay compared with placebo.[85] However, neither of the individual agents performed better than placebo.

***Surgical intervention***

Surgical options include thoracoscopy usually by VATS or full thoracotomy with decortication. VATS is most commonly used to debride multiloculated empyemas or uniloculated empyemas that fail to resolve with antibiotics and tube thoracostomy drainage, as an alternative to instillation of intrapleural fibrinolytics. VATS allows for minimally invasive debridement and drainage and can be followed by or converted to a thoracotomy if adequate pleural fluid drainage and lung expansion are not achieved. When visceral pleural fibrosis does not regress and limits reexpansion of the lung, a total pleurectomy/decortication may be required to achieve lung reexpansion.[86] Open thoracostomy involves a vertical incision through the chest wall with rib resection to permit open drainage at the inferior border of the empyema cavity. A chest tube is left in place; it is gradually advanced outward as the tract closes.

In summary, pulmonary infectious emergencies are responsible for significant morbidity and mortality, and frequently require treatment in Intensive Care Unit. Early aggressive treatment is required to effectively control these infections.

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