Guidelines for the Evaluation and Treatment of Pneumonia

Samuel N. Grief, MD, FCFP[a],*, Julie K. Loza, MD[b]

KEY POINTS

- Pneumonia is a common respiratory infection and warrants careful consideration of antibiotic initiation and choice, along with knowledge of local antibiotic resistance patterns.
- Community-acquired pneumonia afflicts all age groups and although not always bacterial in origin, is clinically versatile, depending on its cause.
- Nonresolving pneumonia may be because of less common pathogens, or feature other conditions, and requires more detailed investigation.
- Pediatric pneumonia is also common, and first-line treatment is still amoxicillin, followed closely by cephalosporins or macrolides.
- Other categories of pneumonia, including mechanically induced (ventilator) or travel/geriatric pneumonia, benefit from astute clinical acumen, proper history and physical examination, and knowledge of microbial causes.

INTRODUCTION

Pneumonia is a leading cause of hospitalization among both adults and children in the United States, accounting for more than 800,000 hospitalizations and more than 400,000 emergency department visits in 2014.[1,2] It is among the most expensive conditions treated in US hospitals with national aggregate costs of $9.5 billion in 2013.[3]

A causal pathogen is often not identified. A 2015 prospective, multi-center study by the Centers for Disease Control and Prevention identified a responsible pathogen in only 38% of cases of community-acquired pneumonia (CAP) in adults requiring hospitalization.[4] CAP is an infection of the lung parenchyma that is acquired outside of

hospitals or extended-care facilities.[5] Viral pathogens were identified in 27% of cases and bacterial pathogens in 14% of cases.[5] In adults of all ages, human rhinovirus and influenza were the most frequently identified viruses.[5] *Streptococcus pneumoniae* is the most common causal bacterium. *Staphylococcus aureus* and *Enterobacteriaceae* were significantly more common among patients requiring intensive care unit (ICU) level care.[4] Other bacteria identified in CAP include *Mycoplasma pneumoniae*, *Chlamydophila pneumoniae*, and *Haemophilus influenzae*.[5] Less common bacterial causes include *Mycobacterium tuberculosis*, *Legionella* sp, and *Pseudomonas aeruginosa*. These and other bacteria may be considered more likely in patients with certain risk factors (**Table 1**).[6]

DIAGNOSIS

A diagnosis of pneumonia should be considered in patients presenting with acute onset fever or chills and cough. The cough may be described as productive. Additional symptoms frequently seen include fatigue, anorexia, and pleuritic chest pain. Important components of a history include recent travel, history of underlying lung disease,

Table 1
Risk factors and infectious causes in community-acquired pneumonia

Risk Factor	Infectious
Agricultural animals	*Coxiella burnetii* (Q fever)
AIDS	*Aspergillus* and *Cryptococcus* species, *Histoplasma capsulatum*, *Haemophilus influenzae*, *Nocardia* species, nontuberculous mycobacteria, *Pneumocystis jiroveci*
Alcoholism (aspiration)	Anaerobic oral flora, *Klebsiella pneumoniae*, *Mycobacterium tuberculosis*, *Streptococcus pneumoniae*
Avian fecal matter	*H. capsulatum*
Chronic obstructive pulmonary disease	*Chlamydophila pneumoniae*, *H. influenzae*, *Legionella* species, *Moraxella catarrhalis*, *Pseudomonas aeruginosa* or other gram-negative rods, *S. pneumoniae*
HIV infection	*H. influenzae*, *M. tuberculosis*, *S. pneumoniae*
Hotel or cruise ship travel (recent)	*Legionella* species
Influenza	*H. influenzae*, influenza and other respiratory viruses, *S. pneumoniae*, *Staphylococcus aureus* (including MRSA)
Intravenous drug use	Anaerobes, *M. tuberculosis*, *S aureus* (including MRSA), *S. pneumoniae*
Pulmonary abscess	Anaerobic oral flora, *M. tuberculosis*, nontuberculous mycobacteria, *S. aureus* (including MRSA)
Travel (national/international)	*Blastomyces dermatitidis*, *Coccidioides* species, *Hantavirus* species Middle East respiratory syndrome, Avian influenza, inter alia

Abbreviations: AIDS, acquired immunodeficiency syndrome; HIV, human immunodeficiency virus; MRSA, methicillin-resistant staphylococcus aureus.

Adapted from Kaysin A, Viera AJ. Community-acquired pneumonia in adults: diagnosis and management. Am Fam Physician 2016;94(9):699; with permission.

and smoking history.[4,6] A study by Diehr and colleagues[7] found that history of alcoholism or bloody sputum have relative risk of 1, so the presence of these findings is not predictive of pneumonia. Physical examination findings frequently appreciated in patients with pneumonia include decreased breath sounds, rales, tactile fremitus, and crackles.[4,8] Tachypnea and hypotension are more worrisome symptoms that may also be seen and require urgent evaluation.[4] It is imperative to maintain a high level of suspicion in immunocompromised or elderly and nursing home patients, because they frequently display fewer overt symptoms of pneumonia when compared with the general population.[8,9]

No individual component of the history or physical examination is useful in diagnosing pneumonia, but the presence of multiple findings is required (**Table 2**). In adults presenting with acute cough, the baseline probability of pneumonia is only 5%. Absence of any vital sign abnormality (blood pressure, heart rate, respiratory rate) reduces the predicted probability of pneumonia to 1%.[8] A chest radiograph should be ordered for any patient with abnormal vital signs defined as temperature higher than 100°F, heart rate higher than 100 bpm, or respiratory rate higher than 20 bpm. Imaging should also be obtained for physical examination abnormalities of crackles or decreased breath sounds in a patient without asthma.[10] Infectious Disease Society of America 2016 Guidelines recommend imaging with a demonstrable infiltrate to confirm the diagnosis of pneumonia and to exclude other causes of cough and fever such as acute bronchitis.[11] Although X-ray imaging is a mainstay of diagnosis of pneumonia, the British Thoracic Society recommends the entire clinical picture should be considered when making a decision to treat.[12] A systematic review found that among patients who are sick enough to be admitted with a clinical diagnosis of CAP but have a normal initial chest radiograph, approximately 1 in 10 will develop radiographic evidence of pneumonia within 72 hours.[8] In such cases, it is appropriate to treat the patient empirically for pneumonia and repeat imaging in 24 to 48 hours.[11] Community resources and access to imaging may also affect decision to treat without imaging.

Routine blood and sputum culture testing is costly and often low-yield.[13] However, more extensive diagnostic testing should be considered in patients who are at risk for infection with unusual pathogens, who are not responding to treatment, or when additional testing is likely to change antibiotic management (**Table 3**).[11,12]

It is reasonable to consider respiratory viral polymerase chain reaction (PCR) to determine viral causes of symptoms, so that inappropriate antibiotic use can be limited. Additional testing for *M. tuberculosis* should be considered in a patient presenting with persistent cough, particularly in the setting of weight loss, malaise, night sweats, or hemoptysis. Additional risk factors for tuberculosis (TB) include

| Table 2 | |
| Predictors of adult pneumonia | |
Score	Likelihood Ratio
≥3	14
≥1	5
≥−1	1.5
<−1	0.22

Add or subtract points as follows: rhinorrhea = −2, sore throat = −1, night sweats = 1, myalgias = 1, sputum all day = 1, respiratory rate >25/min = 2, temperature ≥37.8°C (100°F) = 2.

Adapted from Simel DL, Rennie D. Pneumonia, adult, community-acquired. In: Simel DL, Rennie D, editors. The rational clinical examination: evidence-based clinical diagnosis. New York: McGraw-Hill; 2009; with permission.

Table 3
Indications for further testing

Indication	Blood Culture	Sputum Culture	Legionella UAT	Pneumococcal UAT	Other
ICU admission	X	X	X	X	x[a]
Failure of outpatient antibiotic therapy	—	x	x	X	—
Cavitary infiltrates	X	X	—	—	x[b]
Leukopenia	x	—	—	x	—
Alcohol abuse (current)	x	X	x	x	—
Liver disease	x	—	—	x	—
Lung disease	—	x	—	—	—
Asplenia	x	—	—	x	—
Travel within past 2 wk	—	—	x	—	x[c]
Positive Legionella UAT results	—	x	NA	—	—
Positive pneumococcal UAT result	x	x	—	NA	—
Pleural effusion	x	x	x	x	x[d]

Abbreviations: NA, not applicable; UAT, urinary antigen test.
[a] Endotracheal aspirate if intubated, bronchoscopic alveolar lavage, as needed.
[b] Fungal and tuberculosis cultures.
[c] See Table 1.
[d] Thoracentesis and pleural fluid cultures.
Adapted from Mandell L, Wunderink R, 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(Supplement_2), S40; with permission.

immigration from an endemic country, residing in a homeless shelter, intravenous drug use, or human immunodeficiency virus (HIV) infection. Persons who work with people at high risk for TB infection are also considered high risk.[12,14]

TREATMENT

Most cases of pneumonia can be managed in the outpatient setting. Several severity assessment tools have been developed to help determine appropriate treatment settings. The Pneumonia Severity Index (PSI) considers 20 variables to stratify patients into 1 of 5 risk categories (I–V) based on risk of death within 30 days.[15] Given the number of parameters required, it is not frequently used in general practice. The CURB65 assessment tool was introduced in 2003 by the British Thoracic Society.[16] Similar to the PSI, it calculates risk of 30-day mortality, but instead only uses 5 variables (confusion, urea, respiratory rate, blood pressure, and age >65), with one point awarded for each if present, allowing for greater ease of use.[15,16] The CRB65 can be calculated without blood urea and thus is useful in the outpatient setting. A recent systematic review and meta-analysis found no significant difference in test performance when comparing the 3 severity tools.[15] It was noted that the PSI negative likelihood ratio suggests it may be superior in identifying low-risk patients, and the CURB65 and CRB65 may be superior in identifying high-risk patients.[15] A CURB65 or CRB65 score of 0 or 1 demonstrates low risk of mortality and suggests a patient can be managed in the outpatient setting. A score of 3 or higher should warrant hospital admission. It is always appropriate to consider a patient's social circumstances and treatment wishes when making treatment decisions[12,16] (**Fig. 1**; CURB65 score[12]).

Symptoms/Signs suggestive of CAP

(+/- Chest x-ray)

Criteria met for CAP?

NO – consider other diagnosis

YES

Treat per **CURB 65 score** and clinical judgment

0–1   2   3–5

Home - On oral antibiotics

OR

Hospital admission

(Social situation, co-morbid

conditions)

CURB65 Severity Score

1 point for each:

Confusion

Urea>19 mg/dl

Respiratory Rate>30/min

Blood pressure (SBP<90 or DBP<60)

Age>65

Hospital admission:

Supportive Care

Investigations

Antibiotics

Hospital admission:

Supportive Care, ICU as needed
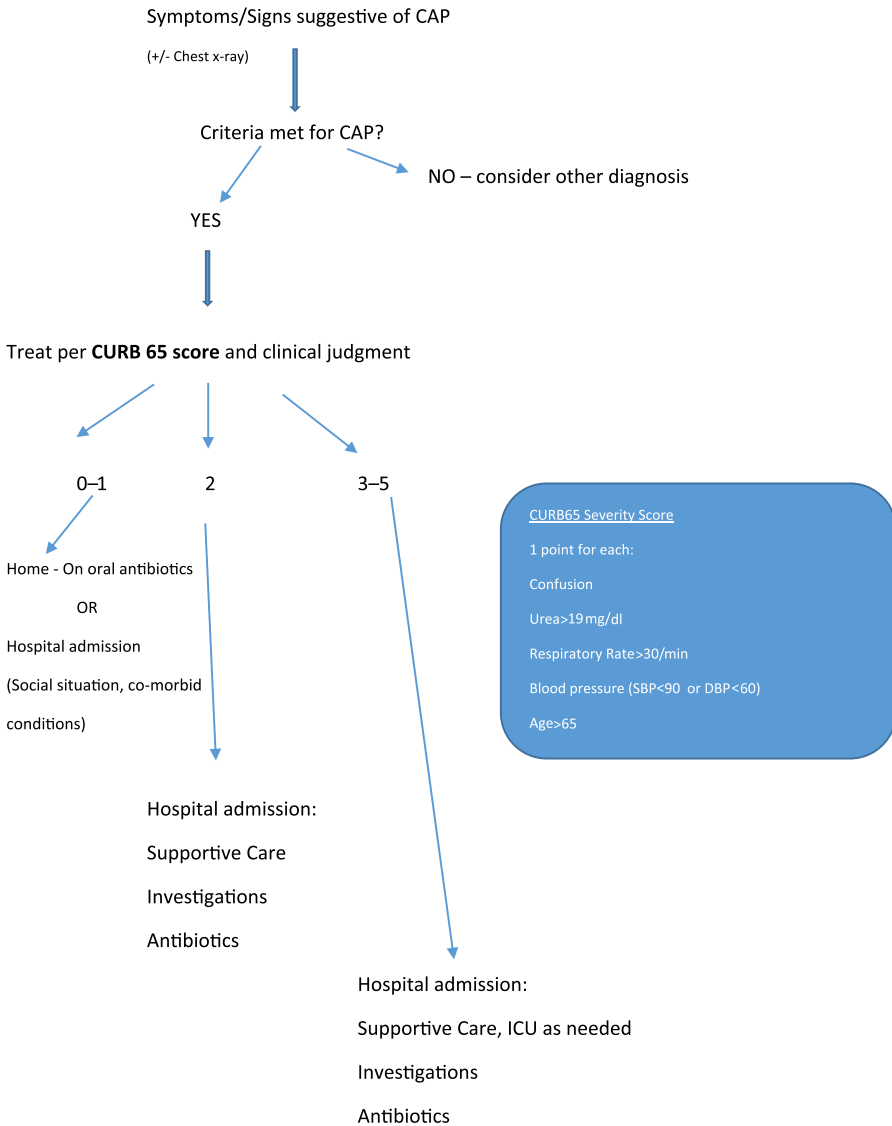
Investigations

Antibiotics

Fig. 1. CURB65 score. (*Adapted from* Lim WS, Baudouin SV, George RC, et al. BTS guidelines for the management of community acquired pneumonia in adults: update 2009. Thorax 2009;64(suppl 3):iii29; with permission.)

When available, treatment of CAP should be guided by local resistance patterns. In previously healthy patients who are appropriate for outpatient treatment, recommended first-line treatment is with a macrolide antibiotic such as azithromycin targeting the most common causal pathogen *S. pneumoniae*. Doxycycline is an alternative option. Patients with comorbidities such as diabetes; chronic heart, lung, renal, or liver disease; alcoholism; asplenia; impaired immune system; or recent antibiotic use within the last 3 months have an increased risk for drug-resistant *S pneumoniae*. As such, a respiratory fluoroquinolone or β-lactam plus a macrolide is recommended (**Table 4**).[11]

Table 4
Outpatient treatment of community-acquired pneumonia

Presence of Comorbidities	Antibiotic Choice
NO	Macrolide or doxycycline
YES	Fluoroquinolone or beta-lactam + macrolide (doxycycline is an alternative for macrolide)

Comorbidities: chronic heart; lung, liver, kidney disease; diabetes; cancer; impaired immune system; alcoholism; asplenia; recent use of antibiotics in previous 3 mo; and risk for multidrug-resistant *S. pneumoniae*.

Adapted from Mandell L, Wunderink R, 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(Supplement 2):S45.

A 2014 Cochrane review found no significant differences in efficacy between antibiotic regimens, although there were differences in adverse effects when comparing antibiotics within a single class.[17] Patients appropriate for inpatient non-ICU treatment should also be treated with a respiratory fluoroquinolone or macrolide with β-lactam. Patients should be treated for a minimum of 5 days and should be clinically stable with resolving symptoms before treatment is discontinued.[11,18] Patients with high severity of infection or with extrapulmonary manifestations may benefit from longer duration of therapy, such as 7 to 10 days or until improving.[11,12]

In recent years, there has been emerging data supporting the use of adjunctive corticosteroids in the inpatient treatment of CAP. As this is an area of research, multiple recent systematic reviews and meta-analyses have been published, some with conflicting findings. A 2011 Cochrane review that included relevant CAP studies through the year 2010 showed that corticosteroid use accelerates time to symptom resolution and clinical stability, with infrequent adverse effects.[19] Similarly, a 2015 systematic review by Siemieniuk and colleagues[20] included studies from 2011 through mid-2015. Their analysis of 13 randomized controlled trials found significantly decreased mortality in severe pneumonia, decreased need for mechanical ventilation, decreased occurrence of acute respiratory distress syndrome, decreased time to clinical stability, and shorter duration of hospitalization.[20] Hyperglycemia requiring treatment occurred more frequently in patients treated with corticosteroids.[20,21] The most recent IDSA and BTS guidelines do not make recommendations regarding the routine use of adjunctive corticosteroid for CAP.[11,12] Given the variations in dose and route of administration, an optimal agent and dose is unknown. Further research is needed to determine steroid dosing and duration, as well as what patient populations are most likely to benefit from its use.[20,21]

There are a large number of studies assessing the role of the infection biomarker procalcitonin in diagnosis and monitoring of patients with bacterial infections.[22] A Cochrane 2017 meta-analysis in the primary care setting concluded that the use of procalcitonin to guide initiation and duration of antibiotic treatment results in lower risks of mortality, lower antibiotic consumption, and lower risk for antibiotic-related side effects.[23] Procalcitonin values too low or too high usually exclude bacterial infection, but not always.[24]

Per practitioner discretion and, depending on patient complexity and other comorbidities, a follow-up appointment after successful management in the primary care setting may be arranged. At this appointment, repeat X-ray imaging to confirm resolution of pneumonia is not indicated if the patient seems clinically well. In patients with persistence of symptoms or who have a high risk of lung cancer (age > 50, >30 pack year smoking history), repeat X-ray imaging or low-dose computerized tomography (CT) scan to screen for lung cancer can be considered.[12]

PREVENTION

In the United States, the pneumococcal conjugate vaccine (PCV13 or Prevnar-13) is recommended for all babies and children younger than 2 years, all adults aged 65 years or older, as well as children and adults aged 2 years through 64 years who are at increased risk for pneumococcal disease due to certain medical conditions.[24] The pneumococcal conjugate vaccine has been shown to have an observed 46% reduction in vaccine-type pneumococcal CAP, persisting for at least 4 years after receiving the vaccine.[25,26] The pneumococcal polysaccharide vaccine (PPSV23 or Pneumovax 23) is recommended for all adults aged 65 years or older, all cigarette smokers aged 19 to 64 years, as well as children and adults aged 2 to 64 years with certain medical conditions.[27] A 2013 Cochrane review found that the polysaccharide vaccine is effective in preventing invasive pneumococcal disease in healthy adults. Vaccine efficacy was, however, poorer in adults with chronic illnesses.[28]

NONRESOLVING PNEUMONIA

Pneumonia is considered "nonresolving" if there is an inadequate clinical response despite antibiotic treatment.[11] The incidence of treatment failure is 6% to 15% and is associated with a 5-fold increase in mortality.[29] IDSA broadly classifies nonresponse into 2 different groups: (1) progressive pneumonia characterized by clinical deterioration and (2) persistent pneumonia with absence or delay of clinical stability.[11] Progressive pneumonia with deterioration is characterized by respiratory failure and/or septic shock and typically occurs within 72 hours. Persistent pneumonia with absent or delayed response is typically considered after a time period of 72 hours, because this is often regarded as the median time required for clinical stability.[11,29]

Concern for nonresponse in a patient with pneumonia should initiate a systematic evaluation of possible causes. Host factors that may explain poor response should be considered, including high initial severity score, risk factors for infection with unusual organisms, underlying comorbidities, or risk factors for multi–drug-resistant pathogens (Table 5).[24] In areas with high prevalence of HIV or TB, testing is

Table 5
BAD OMEN (nonresolving pneumonia)

Disease/Risk Factor Mnemonic	Listing of Diseases/Conditions/Risk Factors
B	Bronchiolitis obliterans/Bronchiectasis/Influenza B
A	Age >60/Aspiration/Anaerobic infection/Abscess/Influenza A/Atypical pathogens (eg, Legionella, Mycoplasma, hMPV, chlamydia)
D	Drug-resistant pneumonia from *S. Pneumoniae*, gram-negative bacteria, MRSA, ESBL/Drug-induced pneumonitis (eg, amiodarone, MTX, nitrofurantoin, cancer biologics)/Delayed resolution from corticosteroids
O	Opportunistic pathogens (eg, Fungi, mold, *Pneumocystis Jiroveci*); anaerobic bacteria. Consider HIV testing.
M	Misdiagnosis (fungal infections, sarcoidosis, TB)
E	Embolism/Empyema/Eosinophilic pneumonia
N	Neoplasm/Nosocomial bacterial pneumonia

Abbreviations: ESBL, extended-spectrum beta-lactamase organisms; hMPV, human metapneumovirus; MTX, methotrexate.
Adapted from Tan L, Louie S. Unresolved acute pneumonia: a "BAD OMEN". Consultant 2017;57(8):502; with permission.

recommended.[30] Results of initial microbiological tests such as blood or sputum cultures should be reviewed, including any sensitivity data. Repeat blood cultures should be obtained in the setting of clinical deterioration. Additional laboratory testing for *S. pneumonia* and *Legionella pneumophila* via urine antigen testing may be performed, because they may remain positive for days after initiating antibiotic treatment. Additional imaging such as chest CT may be beneficial for assessing interval progression or improvement or identifying pleural effusions, lung abscesses, or pulmonary embolism. If pleural effusions are identified in a patient with treatment failure, thoracentesis should be performed to evaluate for empyema. In select patients, bronchoscopy with protected bronchial sampling or bronchoalveolar lavage (BAL) may be beneficial to provide diagnostic information for infectious causes and noninfectious mimics, such as pulmonary eosinophilia, drug-induced pneumonitis, sarcoidosis, or pulmonary fibrosis.[11,29] Primary or metastatic neoplastic lesions obstructing the bronchus may cause accumulation of secretions distal to the obstruction, predisposing to infection. Both Hodgkin and non-Hodgkin lymphoma can present with lung involvement, with typical radiographic findings of hilar or mediastinal adenopathy, but may also have a presenting pattern that suggests infection.[31]

PNEUMONIA IN THE ELDERLY

Elderly patients with pneumonia may not exhibit typical symptoms or physical examination findings seen in younger adults, such as pleuritic chest pain, cough, fever, and leukocytosis.[32] Signs and symptoms more frequently seen in older adults include falls, decreased appetite, or functional impairment.[32] A change in mental status should prompt evaluation for an infectious cause.[9,11] As with any adult, risk factors for atypical or drug-resistant pathogens should guide treatment. Elderly patients with history of stroke or known dysphagia are at an increased risk for aspiration pneumonia. Residents of nursing homes or long-term care facilities are at an increased risk for methicillin-resistant *Staphylococcus aureus* (MRSA) or multidrug-resistant (MDR) pathogens.[32]

TRAVEL

Evaluation of a returned traveler should include the following: appropriate history covering the travel itinerary (location and activities), onset of illness related to travel, vaccines or prophylaxis received, diet, sexual history, and exposure to animals.[30,33] Respiratory tract infections are among the most common health care complaints affecting returned travelers and are diagnosed in up to 24% of returned patients with fever.[30,34] Although upper respiratory tract infections are more common, the severity and possible mortality associated with lower respiratory tract infections such as pneumonia make it a must-not-miss diagnosis in the returned traveler. As in the United States, *S pneumoniae*, *H. influenzae*, and *S. aureus* are the dominant pneumonia isolates in developing countries. It must be considered that bacterial resistance patterns from different countries may differ in these otherwise commonplace bacteria.[34]

Respiratory symptoms occur in up to half of patients with malaria, and the presentation may seem similar to that of pneumonia. Thus, in a patient returning from a malaria-endemic area, blood smear testing for malaria should be performed.[35] Increased time spent at hotels or on cruise ships in a patient presenting with symptoms of pneumonia should increase suspicion for *Legionella*.[30] Travelers returning from East and Southeast Asia, as well as Australia, with a severe pneumonia may have been exposed to *Burkholderia pseudomallei*—the causative agent of melioidosis, which can cause severe necrotizing pneumonia and has 14% to 40% mortality despite appropriate antibiotic therapy.[30] Severe pneumonia may also be because of viruses such as influenza, Middle

Eastern respiratory syndrome, or hantavirus. A returned traveler with pneumonia with eosinophilia should raise suspicion for helminth infection.[30,34]

Histoplasma capsulatum is a dimorphic fungus that is relatively common in North, Central, and South America and given its growth in bird and bat droppings is associated with activities such as cave exploration. *Coccidioides immitis* is endemic in the southwest United States and northern Mexico, as well as smaller areas in Central America. It is spread through inhalation of spores found in the soil. Fungal infection with *H. capsulatum* and *C immitis* are often asymptomatic but may also present as a flulike illness with fever, malaise, and dry cough 1 to 3 weeks after exposure.[34,36]

Ventilator-Associated Pneumonia

Ventilator-associated pneumonia (VAP) is a type of pneumonia that occurs in patients who have been intubated or mechanically ventilated by means of a tracheostomy for at least 48 hours.[37,38] Mechanical ventilation modifies the oropharyngeal and tracheal environment, allowing oral and gastric secretions to enter the lower airways.[37] It is this change in lower respiratory tract bacterial flora that precipitates the beginning of pneumonia.

VAP is common. Approximately 30% of patients who receive mechanical ventilation will develop VAP.[39]

DIAGNOSTIC CRITERIA

VAP should be suspected when signs of pulmonary infection (fever, purulent secretions, leukocytosis) and radiologic evidence (air bronchograms, infiltrates) are present; bacteriologic confirmation usually follows.[40] Sensitivity and specificity of the diagnostic criteria discussed earlier are 69% and 75%, respectively.[40] Other useful diagnostic criteria have been developed, incorporating additional symptoms and similar signs and laboratory/radiologic criteria.[41] Once VAP is clinically suspected, early empirical treatment is favored. Delaying treatment and/or not appropriately covering for the likely microbial culprit are both associated with higher morbidity and mortality.[42–45]

MICROBIOLOGY

Microbial organisms associated with VAP have been identified (**Table 6**). Early versus late-onset VAP organisms have also been documented.[46,47] Acinetobacter, citrobacter, pseudomonas, and klebsiella are the most predominant late-onset organisms, warranting more aggressive antibacterial intervention.[47]

DIAGNOSTIC TESTING

Bacterial confirmation usually requires secretion sampling, either via bronchoscopic or via nonbronchoscopic methods. Obtaining pleural fluid, when present, under ultrasound guidance, is recommended.[37] Endotracheal aspirates are easily retrieved but have a high false-positive rate in ICU patients due to airway colonization.[37] Bronchoscopic retrieval of distal airway specimens via BAL or protected-specimen brush techniques is the best, but requires a trained bronchoscopist.[37]

ANTIBIOTIC TREATMENT

Selection of antibiotics is typically done empirically and based on whether the patient has any risk factors for MDR pathogens (**Table 7**) and whether onset of VAP is early (defined as within first 4 days of being in the ICU) or late (5 days or later).[37,38,48]

Table 6	
Bacterial distribution in ventilator-associated pneumonia	
Bacterial Organism	**Percentage**
Citrobacter freundii	53
Klebsiella pneumoniae	13
Staphylococcus aureus	9.5
Acinetobacter baumannii	7.5
Pseudomonas aeruginosa	3.8
P. aeruginosa + C. freundii	3.8
Coagulase-negative Staphylococci	1.9
Escherichia coli	1.9
Morganella morganii	1.9
Proteus vulgaris	1.9
P. aeruginosa + K. pneumoniae	1.9

Adapted from Thakuria B, Singh P, Agrawal S, et al. Profile of infective microorganisms causing ventilator-associated pneumonia: a clinical study from resource limited intensive care unit. J Anaesthesiol Clin Pharmacol 2013;29(3):363; with permission.

Empirical treatment should also be determined as a result of knowledge of local distribution of pathogens and their antimicrobial susceptibility patterns.[49] Early-onset VAP without MDR risk factors typically should be prescribed one of the following antibiotic options[37]:

- Ceftriaxone
- Fluoroquinolone
- Ampicillin-sulbactam
- Ertapenem

For late-onset and/or MDR factor patients, appropriate antibiotic options would include one or more of the following[37]:

Table 7		
Risk factors for multidrug-resistant ventilator-associated pneumonia		
Risk Factors for MDR Pathogens	**Risk Factors for MDR Pseudomonas and Other Gram-Negative Bacilli**	**Risk Factors for MRSA**
IV antibiotic use within previous 3 mo	Treatment in an ICU setting with the following:	Treatment in a medical ward/ICU in which:
Sepsis accompanying VAP	1. >10% of gram-negative isolates are resistant to one or more antibiotics indicated for VAP	1. >10%–20% of *Staphylococcus aureus* isolates are MRSA
Adult respiratory distress syndrome before VAP		
Late-onset VAP (5 d or more in ICU/hospital)	2. Local antimicrobial susceptibilities are unknown	2. Prevalence of MRSA is unknown
Dialysis just before VAP		

Abbreviations: IV, intravenous; MDR, multidrug-resistant; MRSA, methicillin-resistant *S. aureus*; VAP, ventilator-associated pneumonia.

Adapted from Kalil AC, Metersky ML, Klompas M, et al. Management of adults with hospital-acquired and ventilator-associated pneumonia: 2016 clinical practice guidelines by the Infectious Diseases Society of America and the American Thoracic Society. Clin Infect Dis 2016;63:e61; with permission.

- Antipseudomonal cephalosporins (eg, Cefepime, ceftazidime)
- Antipseudomonal carbapenems (imipenem or meropenem)
- Beta-lactam/beta-lactamase inhibitors (piperacillin-tazobactam) with an antipseudomonal fluoroquinolone (ciprofloxacin) or aminoglycoside plus linezolid or vancomycin (if MRSA risk factors are present)
- Telavancin is indicated for VAP for susceptible isolates of S. aureus when other therapies are not suitable.

Dose and frequency of administration of the antibiotic choices discussed earlier are documented extensively elsewhere.[38] Atypical antibiotic choices, such as colistin, polymyxin B, telavancin, inter alia, are rarely indicated but can be used when antimicrobial resistance warrants these agents.[48] Typically, consultation with an infectious disease physician or clinical pharmacist with expertise and familiarity when using these drugs is a sine qua non.[48]

Pediatric Pneumonia

Epidemiology
Pneumonia is a very common affliction of childhood. Pneumonia accounts for 13% of infectious illnesses in infants and toddlers younger than 2 years.[50] Worldwide, approximately 150 million new cases of pneumonia occur annually among children younger than 5 years.[50] Pneumonia is the leading cause of death in children younger than 5 years in developing countries, accounting for 16% of all deaths of children younger than 5 years and killing 920,136 children in 2015.[51,52]

Most childhood pneumonia (CP) can be treated in the outpatient setting. The rate of hospitalization for CP through age 18 years varies per year, but in 2006 it was 201.1 per 100 000.[53] Infants younger than 1 year had the highest rate of hospitalization (912.9 per 100 000), whereas children aged 13 to 18 years had the lowest rate (62.8 per 100 000).[53]

Diagnosis
Signs and symptoms of CP are often nonspecific and depend on several factors including age, microbial organism, and underlying health of the patient. Clinical acumen is key to successfully diagnosing CP. The universal symptom of CP is cough. Other symptoms may include chest pain, headache, arthralgia, nausea, and abdominal pain.[54] Most common signs to look for include fever, tachypnea, labored breathing, rhonchi, crackles, and wheezing.[54] Other physical signs to identify include grunting, nasal flaring, and chest retractions because these increase the likelihood of CP.[55] Diagnostic testing is usually performed, when available, and would include assessment of oxygen saturation by pulse oximetry, chest radiograph, complete blood cell count, respiratory microbial panel by PCR, ultrasound of the chest (when medically indicated), and cultures. Disagreement about whether blood cultures are warranted exists in the literature. As per a recent study, blood cultures have not been shown to assist with clinical management in children hospitalized with pneumonia.[56] The Infectious Diseases Society of America, however, recommends blood cultures for all hospitalized children with pneumonia.[57]

Etiology of pneumonia
Etiologic microbial organisms differ, depending on age of the child. In infants, toddlers, and preschoolers, viruses predominate (**Table 8**). Less common bacterial organisms may infect newborns (see **Table 8**). In older children, bacteria are the more common culprit (**Table 9**). Atypical organisms may be involved when children are immunocompromised or have other underlying comorbidities (see **Table 9**).

Table 8	
Etiology of childhood pneumonia (age 0–5 years)	
Viruses	**Bacteria**
RSV	*Streptococcus pneumoniae*
Parainfluenza types 1, 2, 3	Hemophilus influenzae type B
Influenza A and B	Streptococcus pyogenes
Adenovirus	*Staphylococcus aureus*
Rhinovirus	Mycoplasma pneumoniae
Coronavirus	Chlamydia pneumoniae/Chlamydia trachomatis
hMPV	Bordetella pertussis
HSV	***Escherichia coli***
VZV	***Klebsiella pneumoniae***
CMV	***Listeria monocytogenes***
Enterovirus	***Group B Streptococcus***

Abbreviations: CMV, cytomegalovirus; hMPV, human metapneumovirus; HSV, herpes simplex virus; RSV, respiratory syncytial virus; VZV, varicella zoster virus.
 Italicized/bolded are more common in newborns (age 0–30 days).
 Data from Bennett NJ, Domachowske J, Steele R. Pediatric pneumonia. Medscape. 2017; and Stuckey-Schrock K, Hayes BL, George CM. Community-acquired pneumonia in children. Am Fam Physician 2012;86(7):661–7.

Outpatient versus inpatient

In order to provide optimal care to a child with pneumonia, it is important to determine the severity of the pneumonia and the child's clinical status. Most children will not require inpatient admission; criteria exist to help stratify severity of pneumonia and necessity of hospitalization (**Box 1** and **2**).

Antibiotics

Choosing an antibiotic for CP is initially always an empirical process and based on local and regional microbial susceptibility and resistance patterns, along with the child's age, immunization status, and any underlying, preexisting health

Table 9		
Causes of childhood pneumonia (>5 years old)		
Bacteria	**Viruses**	**Atypical Organisms**
Mycoplasma pneumoniae	CMV	Aspergillus
Streptococcus pneumoniae	Influenza A and B	*Pneumocystis jirovecii*
Staphylococcus aureus	Rhinovirus	*Pseudomonas aeruginosa*
Streptococcus pyogenes	Adenovirus	*Burkholderia cepacia*
Chlamydia pneumoniae	RSV	*Histoplasma capsulatum*
Hemophilus influenzae type B	Parainfluenza	*Cryptococcus neoformans*
	hMPV	*Blastomyces dermatitidis*
	Enterovirus	*Mycobacterium tuberculosis*
		Legionella pneumophila
		Oral anaerobes (aspiration)

Abbreviations: CMV, cytomegalovirus; hMPV, human metapneumovirus; RSV, respiratory syncytial virus.
 Data from Refs.[1,5,9]

Box 1
Criteria for childhood pneumonia hospitalization

Infants younger than 3 to 6 months with suspected bacterial CAP

Suspected or documented CAP caused by a pathogen with increased virulence, such as community-associated methicillin-resistant *Staphylococcus aureus*

Temperature greater or equal to 38.5 C (101.3 F)

Children and infants for whom there is concern about careful observation at home or who are unable to comply with therapy or unable to be followed-up

Children and infants who have respiratory distress and hypoxemia (oxygen saturation <92%) (see **Table 2**)

Children and infants with comorbidities (eg, asthma, cystic fibrosis, congenital heart disease, diabetes mellitus, neuromuscular disease)

Poor feeding and/or signs of dehydration

Abbreviation: CAP, community-acquired pneumonia.
  Modified from Bradley JS, Byington CL, Shah SS, et al. The management of community-acquired pneumonia in infants and children older than 3 months of age: clinical practice guidelines by the Pediatric Infectious Diseases Society and the Infectious Diseases Society of America. Clin Infect Dis 2011;53(7):e29; with permission.

---

conditions.[50,54,58,59] Most children can be treated with oral antibiotics in the outpatient setting. First-line and preferred agent is still amoxicillin.[50,54,57,59] Alternative agents are cephalosporins and macrolide antibiotics; however, increasing resistance to penicillin derivatives and macrolides should be noted[60] (**Table 10**). Quinolones can be considered in cases where there are no reasonable alternatives due to MDR pathogens or when an oral antibiotic is deemed optimal.[61] Quinolones

---

Box 2
Signs of respiratory distress

Tachypnea: RR

Age 0 to 2 months: greater than 60; age 2 to 12 months: greater than 50; age 1 to 5 years: greater than 40; age greater than 5 years: greater than 20

Dyspnea

Retractions: suprasternal, intercostal, or subcostal

Grunting

Nasal flaring

Apnea

Altered mental status

Pulse oximetry measurement less than 90% on room air

Abbreviation: RR, respiratory rate.
  Adapted from Bradley JS, Byington CL, Shah SS, et al. The management of community-acquired pneumonia in infants and children older than 3 months of age: clinical practice guidelines by the Pediatric Infectious Diseases Society and the Infectious Diseases Society of America. Clin Infect Dis 2011;53(7):e28; with permission.

Table 10
Outpatient childhood pneumonia antibiotic treatment guidelines

Age	Preferred/First-Line	Alternative/Second-Line
0–5 y		
Viral	No treatment	Antiviral against influenza
Bacterial	Amoxicillin	Amoxicillin-clavulanate/ third-generation cephalosporin
Atypical bacterial	Macrolide	Consult infectious disease
Allergy to any of the above	Third-generation cephalosporin/clindamycin	Quinolone
5–16 y		
Viral	No treatment	Antiviral against influenza
Bacterial	Amoxicillin	Amoxicillin-clavulanate/ third-generation cephalosporin
Atypical bacterial	Macrolide or doxycycline	Quinolone if older than 8 years and suspect MDR organism
Allergy to any of the above	Third-generation cephalosporin/clindamycin	Quinolone

Adapted from Cincinnati Children's Hospital Medical Center. Evidence-based care guideline. Community acquired pneumonia in children 60 days through 17 years of age. Available at: https://www.idsociety.org/uploadedFiles/IDSA/Guidelines-Patient_Care/PDF_Library/2011%20CAP% 20in%20Children.pdf Accessed February 20, 2018; with permission.

have been linked to development of childhood tendonitis/tendinopathy, yet recent literature indicates these disabling side effects are rare.[61,62] Inpatient treatment guidelines have also been established (**Table 11**). Isolation of the particular microbial organism is ideal, but not required, in order to determine duration of therapy. Uncomplicated pneumonia treatment in the outpatient setting usually should last 5 to 10 days.[54] Inpatient admission for pneumonia warrants longer duration of antibiotic therapy, typically 7 to 10 days of combined parenteral and oral therapy or at least 1 week after becoming afebrile.[58] Complicated cases of pneumonia will require a minimum of 2 weeks of therapy once lack of fever is confirmed and may be extended for up to 4 weeks.[58] The switch from parenteral to oral therapy may occur after 24 to 48 hours of documented lack of fever but is not always practical in complicated and/ or ICU-admitted patients.[63]

SUMMARY

Pneumonia is a common, well-recognized respiratory infection seen in primary care settings. Triage of the usual presenting symptoms will generally set into motion a typical course of action, including physical examination and possibly imaging to confirm clinical suspicion. Further testing depends on treatment venue (outpatient vs inpatient) and other specific criteria (see **Table 3**). Empirical antibiotic therapy is the cornerstone of treatment, and knowledge of local and regional microbial susceptibility and resistance will bolster the success rate of outpatient management of pneumonia, regardless of demographic and/or accompanying morbidities. Special circumstances and scenarios that may occur, including nonresolving pneumonias, pediatric or geriatric populations, travel-related infections, among others, will necessitate a more careful attention to history, physical examination, and antibiotic selection.

Table 11
Inpatient childhood pneumonia antibiotic treatment guidelines

Age/Category	Preferred/First-Line	Alternative/Second-Line
0–6 mo		
Bacterial	IV penicillin derivative and third-generation cephalosporin	Aminoglycoside with PCN derivative; macrolide if suspect atypical organism
6 mo–5 y		
Bacterial	IV penicillin derivative (PCN or ampicillin)	Third-generation cephalosporin
MRSA	Vancomycin or clindamycin (in addition to beta-lactam antibiotic)	Vancomycin or clindamycin (in addition to beta-lactam antibiotic)
Atypical bacterial infection	Macrolide	Macrolide (in addition to beta-lactam antibiotic)
Allergy to any of the above	Third-generation cephalosporin/ clindamycin	Quinolone
5–16 y		
Bacterial	IV penicillin derivative (PCN or ampicillin)	Third-generation cephalosporin
MRSA	Vancomycin or clindamycin (in addition to beta-lactam antibiotic)	Vancomycin or clindamycin (in addition to beta-lactam antibiotic); linezolid in children aged 12 y or older
Atypical bacterial infection	Macrolide	Macrolide (in addition to beta-lactam antibiotic)
Allergy to any of the above	Third-generation cephalosporin/ clindamycin	Quinolone
Severe pneumonia/ ICU admission	Third-generation cephalosporin and macrolide/vancomycin + third-gen ceph + macrolide	Third-generation cephalosporin and doxycycline/vancomycin + third-gen ceph + macrolide + (optional) Nafcillin + antiviral

Abbreviations: Ceph, cephalosporin; IV, intravenous; PCN, penicillin.
Adapted from Cincinnati Children's Hospital Medical Center. Evidence-based care guideline. Community acquired pneumonia in children 60 days through 17 years of age. Available at: file:///C:/Users/sgrief/Downloads/Community%20Acquired%20Pneumona%20Great%20001.pdf. Accessed February 20, 2018; with permission.

REFERENCES

1. McDermott KW, Elixhauser A, Sun R. Trends in hospital inpatient stays in the United States, 2005-2014. HCUP statistical brief #225. Rockville (MD): Agency for Healthcare Research and Quality; 2017. Available at: https://www.hcup-us.ahrq.gov/reports/statbriefs/sb225-Inpatient-US-Stays-Trends.pdf.
2. Rui P, Kang K. National Hospital Ambulatory Medical Care Survey: 2014 emergency department summary tables. Available at: http://www.cdc.gov/nchs/data/ahcd/nhamcs_emergency/2014_ed_web_tables.pdf. Accessed January 16, 2018.
3. Torio C, Moore B. National inpatient hospital costs: the most expensive conditions by payer, 2013. HCUP statistical brief #204. Rockville (MD): Agency for Healthcare Research and Quality; 2016. Available at: http://www.hcup-us.ahrq.gov/reports/statbriefs/sb204-Most-Expensive-Hospital-Conditions.pdf.

4. Jain S, Self WH, Wunderink RG, et al. Community-acquired pneumonia requiring hospitalization among U.S. adults. N Engl J Med 2015;373(5):415–27.

5. Cisneros ED, Lazarte SM. General infectious diseases. In: De Fer T, Sateia H, editors. The Washington manual of outpatient internal medicine. Philadelphia: Lippincott Williams & Wilkins; 2015. p. 523–6.

6. Kaysin A, Viera AJ. Community- acquired pneumonia in adults: diagnosis and management. Am Fam Physician 2016;94(9):698–706.

7. Diehr P, Wood RW, Bushyhead J, et al. Prediction of pneumonia in outpatients with acute cough: a statistical approach. J Chronic Dis 1984;37(3):215–25.

8. Simel DL, Metlay JP. Pneumonia, adult, community-acquired. In: Simel DL, Rennie D, editors. The rational clinical examination: evidence-based clinical diagnosis. New York: McGraw-Hill; 2009. Available at: http://jamaevidence.mhmedical.com.proxy.cc.uic.edu/content.aspx?bookid=845&sectionid=61357585. Accessed December 17, 2017.

9. Casey C, Fullerton M, Somerville N. Common questions about pneumonia in nursing home residents. Am Fam Physician 2015;92(7):612–20.

10. Ebell MH. Predicting pneumonia in adults with respiratory illness. Am Fam Physician 2007;76(4):560–2.

11. Mandell L, Wunderink R, 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(Supplement 2):S27–72.

12. Lim W, Baudouin S, George R, et al. BTS guidelines for the management of community acquired pneumonia in adults: update 2009. Thorax 2009;64(Suppl 3):iii1–55.

13. Gupta D, Agarwal R, Aggarwal AN, et al. Guidelines for diagnosis and management of community- and hospital-acquired pneumonia in adults: joint ICS/NCCP(I) recommendations. Lung India 2012;29(Suppl 2):S27–62.

14. Tuberculosis (TB) | CDC. Cdcgov. 2018. Available at: https://www.cdc.gov/tb/default.htm. Accessed February 24, 2018.

15. Chalmers J, Singanayagam A, Akram A, et al. Severity assessment tools for predicting mortality in hospitalised patients with community-acquired pneumonia. Systematic review and meta-analysis. Thorax 2010;65(10):878–83.

16. Lim WS, van der Eerden MM, 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.

17. Pakhale S, Mulpuru S, Verheij TJM, et al. Antibiotics for community-acquired pneumonia in adult outpatients. Cochrane Database Syst Rev 2014;2014(10):CD002109.

18. Uranga A, España P, Bilbao A, et al. Duration of antibiotic treatment in community-acquired pneumonia. JAMA Intern Med 2016;176(9):1257.

19. Chen Y, Li K, Pu H, et al. Corticosteroids for pneumonia. Cochrane Database Syst Rev 2011;(3):CD007720.

20. Siemieniuk R, Alonso-Coello P, Guyatt G. Corticosteroid therapy for patients hospitalized with community-acquired pneumonia. Ann Intern Med 2016;164(9):636.

21. Feldman C, Anderson R. Corticosteroids in the adjunctive therapy of community-acquired pneumonia: an appraisal of recent meta-analyses of clinical trials. J Thorac Dis 2016;8(3):E162–71.

22. Sager R, Kutz A, Mueller B, et al. Procalcitonin-guided diagnosis and antibiotic stewardship revisited. BMC Med 2017;15(1):15.

23. Schuetz P, Wirz Y, Sager R, et al. Procalcitonin to initiate or discontinue antibiotics in acute respiratory tract infections. Cochrane Database Syst Rev 2017;(10):CD007498.
24. Tan L, Louie S. Unresolved Acute Pneumonia: a "BAD OMEN". Consultant 2017;500–3.
25. Cdc.gov. Pneumococcal vaccination | what you should know | CDC. [online]. 2017. Available at: https://www.cdc.gov/vaccines/vpd/pneumo/public/index.html. Accessed December 14, 2017.
26. Bonten M, Huijts SM, Bolkenbaas M, et al. Polysaccharide conjugate vaccine against pneumococcal pneumonia in adults. N Engl J Med 2015;372(12): 1114–25.
27. Centers for Disease Control and Prevention. Updated recommendations for prevention of invasive pneumococcal disease among adults using the 23-valent pneumococcal polysaccharide vaccine (PPSV23). MMWR Morb Mortal Wkly Rep 2010;59:1102–5.
28. Moberley S, Holden J, Tatham DP, et al. Vaccines for preventing pneumococcal infection in adults. Cochrane Database Syst Rev 2013;(1):CD000422.
29. Sialer S, Liapikou A, Torres A. What is the best approach to the nonresponding patient with community-acquired pneumonia? Infect Dis Clin North Am 2013; 27(1):189–203.
30. Trimble A, Moffat V, Collins A. Pulmonary infections in the returned traveler. Pneumonia (Nathan) 2017;9:1.
31. Black A. Non-infectious mimics of community-acquired pneumonia. Pneumonia 2016;8:2.
32. Faverio P, Aliberti S, Bellelli G, et al. The management of community-acquired pneumonia in the elderly. Eur J Intern Med 2014;25(4):312–9.
33. Centers for Disease Control and Prevention. CDC yellow book 2018: health information for international travel. New York: Oxford University Press; 2017.
34. Meltzer E, Schwartz E. Travel-related respiratory infections. In: Schwartz E, editor. Tropical diseases in travelers. Hoboken (NJ): Wiley-Blackwell; 2009. p. 413–26.
35. Fairley JK. General approach to the returned traveler. In: Chapter 5: post-travel evaluation. Centers for disease control and prevention. Available at: https://wwwnc.cdc.gov/travel/yellowbook/2018/post-travel-evaluation/general-approach-to-the-returned-traveler. Accessed February 26, 2018.
36. Segel MJ, Schwartz E. Histoplasmosis and other endemic fungal infections. In: Schwartz E, editor. Tropical diseases in travelers. Hoboken (NJ): Wiley-Blackwell; 2009. p. 282–93.
37. Amanullah S, Mosenifar Z. Ventilator-associated pneumonia overview of nosocomial pneumonias. Medscape 2015.
38. File TM. Treatment of hospital-acquired and ventilator-associated pneumonia in adults. UpToDate 2018.
39. Cook DJ, Walter SD, Cook RJ, et al. Incidence of and risk factors for ventilator-associated pneumonia in critically ill patients. Ann Intern Med 1998;129(6): 433–40.
40. Fabregas N, Ewig S, Torres A, et al. Clinical diagnosis of ventilator-associated pneumonia revisited: comparative validation using immediate post-mortem lung biopsies. Thorax 1999;54(10):867–73.
41. Horan T, Gaynes R. Survillence of nosocomial infection. In: Mayhall C, editor. Hospital epidemiology and infection control. 3rd edition. Philadelphia: Lippincott Williams and Wilkins; 2004. p. 1659–702.

42. El Kuti, Patel AA, Coleman CI. Impact of inappropriate antibiotic therapy on mortality in patients with ventilator-associate pneumonia and blood stream infection: a meta-analysis. J Crit Care 2008;23:91.

43. Muscedere JG, Shorr AF, Jiang X, et al. The adequacy of timely empiric antibiotic therapy for ventilator-associate pneumonia: an important determinant of outcome. J Crit Care 2012;27:322.e7.

44. Paul M, Shani V, Muchtar E, et al. Systematic review and meta-analysis of the efficacy of appropriate empiric antibiotic therapy for sepsis. Antimicrob Agents Chemother 2010;54:4851.

45. Swanson JM, Wells DL. Empirical antibiotic therapy for ventilator-associated pneumonia. Antibiotics (Basel) 2013;2:339.

46. Thakuria B, Singh P, Agrawal S, et al. Profile of infective microorganisms causing ventilator-associated pneumonia: A clinical study from resource limited intensive care unit. J Anaesthesiol Clin Pharmacol 2013;29(3):361–6.

47. Rello J, Torres A. Microbial causes of ventilator-associated pneumonia. Semin Respir Infect 1996;11(1):24–31.

48. Kalil AC, Metersky ML, Klompas M, et al. Management of adults with hospital-acquired and ventilator-associated pneumonia: 2016 clinical practice guidelines by the Infectious Diseases Society of America and the American Thoracic Society. Clin Infect Dis 2016;63:e61.

49. Beardsley JR, Williamson JC, Johnson JW, et al. Using local microbiologic data to develop institution-specific guidelines for the treatment of hospital-acquired pneumonia. Chest 2006;130:787.

50. Bennett NJ, Domachowske J, Steele R. Pediatric pneumonia. Medscape 2017.

51. Black RE, Cousens S, Johnson HL, et al, Child Health Epidemiology Reference Group of WHO and UNICEF. Global, regional, and national causes of child mortality in 2008: a systematic analysis. Lancet 2010;375(9730):1969–87.

52. World Health Organization Pneumonia. Fact sheet No. 331. 2016. Available at: http://www.who.int/mediacentre/factsheets/fs331/en/index.html. Accessed February 20, 2018.

53. Lee GE, Lorch SA, Sheffler-Collins S, et al. National hospitalization trends for pediatric pneumonia and associated complications. Pediatrics 2010;126:204–13.

54. Stuckey-Schrock K, Hayes BL, George CM. Community-acquired pneumonia in children. Am Fam Physician 2012;86(7):661–7.

55. Margolis P, Gadomski A. The rational clinical examination. Does this infant have pneumonia? JAMA 1998;279(4):308–13.

56. Neuman MI, Hall M, Lipsett SC, et al. Utility of blood culture among children hospitalized with community-acquired pneumonia. Pediatrics 2017;140(3) [pii: e20171013].

57. Bradley JS, Byington CL, Shah SS, et al. The management of community-acquired pneumonia in infants and children older than 3 months of age: clinical practice guidelines by the Pediatric Infectious Diseases Society and the Infectious Diseases Society of America. Clin Infect Dis 2011;53(7):e25–76.

58. Barson WJ. Pneumonia in children: inpatient treatment. 2018. Available at: http://www.uptodate.com/. Accessed January 16, 2018.

59. Cincinnati Children's Hospital Medical Center. Evidence-based care guideline. Community acquired pneumonia in children 60 days through 17 years of age. Available at: file:///C:/Users/sgrief/Downloads/Community%20Acquired%20Pneumona%20Great%20001.pdf. Accessed February 20, 2018.

60. Neuman MI, Kelley M, Harper MB, et al. Factors associated with antimicrobial resistance and mortality in pneumococcal bacteremia. J Emerg Med 2007; 32(4):349–57.
61. Available at: http://www.aappublications.org/news/aapnewsmag/2016/10/31/Fluoroquinolones103116.full.pdf. Accessed February 20, 2018.
62. Available at: https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/safety-reviews/summary-safety-review-fluoroquinolones-assessing-potential-risk-persistent-disabling-effects.html. Accessed February 20, 2018.
63. Dagan R, Syrogiannopoulos G, Ashkenazi S, et al. Parenteral-oral switch in the management of pediatric pneumonia. Drugs 1994;47(Suppl 3):43.