Treatment of community-acquired pneumonia in adults in the outpatient setting

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INTRODUCTION — Community-acquired pneumonia (CAP) is defined as an acute infection of the pulmonary parenchyma in a patient who has acquired the infection in the community, as distinguished from hospital-acquired (nosocomial) pneumonia. A third category of pneumonia, designated "healthcare-associated pneumonia," is acquired in other healthcare facilities such as nursing homes, dialysis centers, and outpatient clinics.

CAP is a common and potentially serious illness. It is associated with considerable morbidity and mortality, particularly in elderly patients and those with significant comorbidities [1,2]. (See "Prognosis of community-acquired pneumonia in adults").

The treatment of CAP in adults in the outpatient setting will be reviewed here. A variety of other important issues related to CAP are discussed separately. These include:

- The diagnostic approach to patients with CAP. (See "Diagnostic approach to community-acquired pneumonia in adults").
- How one makes the decision to admit patients with CAP to the hospital. (See "Community-acquired pneumonia in adults: Risk stratification and the decision to admit").
- Treatment recommendations for CAP in patients requiring hospitalization. (See "Treatment of community-acquired pneumonia in adults who require hospitalization").
- Treatment recommendations for patients with healthcare-associated pneumonia. (See "Treatment of hospital-acquired (nosocomial); ventilator-associated; and healthcare-associated pneumonia in adults").
- The evidence for efficacy of different antibiotic medications in the empiric treatment of CAP and issues related to drug resistance. (See "Antibiotic studies for the treatment of community-acquired pneumonia in adults").
- The epidemiology and microbiology of CAP. (See "Epidemiology, pathogenesis, and microbiology of community-acquired pneumonia in adults").
- Pneumonia in special populations, such as aspiration pneumonia and immunocompromised patients. (See "Aspiration pneumonia in adults" and see "Common pulmonary infections in immunocompromised patients").

INDICATIONS FOR HOSPITALIZATION — Determination of whether a patient with CAP can

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be safely treated as an outpatient or requires hospitalization is essential before selecting an antibiotic regimen. Severity of illness is the most critical factor in making this determination, but other factors should also be taken into account. These include ability to maintain oral intake, likelihood of compliance, history of substance abuse, cognitive impairment, living situation, and patient functional status. These issues with appropriate references are discussed in detail elsewhere. (See "Community-acquired pneumonia in adults: Risk stratification and the decision to admit").

Summarized briefly, prediction rules have been developed to assist in the decision of site of care for CAP. The two most commonly used prediction rules are the Pneumonia Severity Index (PSI) and CURB-65. The PSI is better studied and validated, but requires a more complicated assessment.

CURB-65 uses five prognostic variables:

- Confusion (based upon a specific mental test or disorientation to person, place, or time)
- Urea (blood urea nitrogen in the United States) >7 mmol/L (20 mg/dL)
- Respiratory rate >30 breaths/minute
- Blood pressure [BP] (systolic <90 mmHg or diastolic <60 mmHg)
- Age >65 years

The authors of the original CURB-65 report suggested that patients with a CURB-65 score of 0 to 1, who comprised 45 percent of the original cohort and 61 percent of the later cohort, were at low risk and could probably be treated as outpatients; those with a score of 2 should be admitted to the hospital, and those with a score of 3 or more should be assessed for ICU care, particularly if the score was 4 or 5.

A simplified version (CRB-65), which does not require testing for blood urea nitrogen, may be appropriate for decision-making in primary care practitioners' offices. With either version, admission to the hospital is recommended if one or more points are present.

Clinical judgment should be used for all patients, incorporating the prediction rule scores as a component of the decision for hospitalization or intensive care unit admission, but not as an absolute determinant [3] .

PRINCIPLES OF ANTIMICROBIAL THERAPY — CAP can be caused by a variety of pathogens, with bacteria being the most common identifiable cause (show figure 1A-1C) [2,4,5] . The choice of initial therapy is complicated by the emergence of antibiotic resistance among Streptococcus pneumoniae, the most common bacterium responsible for CAP. (See "Epidemiology, pathogenesis, and microbiology of community-acquired pneumonia in adults" , section on Microbiology, and see "Antibiotic studies for the treatment of community-acquired pneumonia in adults" , section on Drug resistance and choice of therapy).

Empiric therapy — Antibiotic therapy is typically begun on an empiric basis, since the causative organism is not identified in an appreciable proportion of cases of CAP treated in the outpatient setting (show figure 2) [2,6] . In addition, the clinical features and chest radiographic findings are not sufficiently specific to determine etiology and influence treatment decisions. The sputum Gram stain can be useful for directing the choice of initial therapy if performed on a good quality sample and interpreted by skilled examiners using appropriate criteria [2] . (See "Diagnostic approach to community-acquired pneumonia in adults" , section on Sputum).

The 2007 Infectious Diseases Society of America/American Thoracic Society (IDSA/ATS) guidelines on the management of community-acquired pneumonia suggest that routine tests to identify an etiology for CAP are optional for patients who do not require hospitalization [2] . This recommendation is based in part upon the low rate of failure of empiric therapy in patients with CAP treated in the outpatient setting. The efficacy of empiric therapy was illustrated in a study of over 700 ambulatory patients treated for CAP in one of six emergency departments seen from November 2000 through April 2001, in which empiric antibiotics (a macrolide or fluoroquinolone in >88 percent) were almost universally effective, with only 2.2 percent requiring hospitalization within three weeks of initial emergency department visit [7] .

In contrast, testing for a microbial diagnosis is important in clinical or epidemiologic settings suggesting possible infection with an organism that requires treatment different from standard empiric regimens. These include Legionella species, Mycobacterium tuberculosis, influenza A and B or avian influenza, community-acquired methicillin-resistant Staphylococcus aureus (CA-MRSA), or agents of bioterrorism [2] . (See "Diagnostic approach to community-acquired pneumonia in adults" and see "Sputum cultures" , section on Community-acquired pneumonia).

The selection of antimicrobial regimens for empiric therapy is based upon a number of factors, including:

- The most likely pathogen(s). (See "Common pathogens" below).
- Clinical trials proving efficacy. (See "Antibiotic studies for the treatment of community-acquired pneumonia in adults").
- Risk factors for antimicrobial resistance. The choice of empiric therapy must take into account the emergence of antibiotic resistance among Streptococcus pneumoniae, one of the most common bacteria responsible for CAP. (See "Risk factors for drug resistance" below).
- Medical comorbidities that may influence the likelihood of a specific pathogen and may be a risk factor for treatment failure.

Additional factors that may affect the choice of antimicrobial regimen include the potential for inducing antimicrobial resistance, pharmacokinetic and pharmacodynamic properties, safety profile, and cost [8] .

Common pathogens — Although a variety of bacterial pathogens can cause CAP, a limited number are responsible for the majority of cases. (See "Epidemiology, pathogenesis, and microbiology of community-acquired pneumonia in adults" , section on Microbiology).

With respect to patients treated in the outpatient setting, the most frequently isolated pathogens are Streptococcus pneumoniae, Mycoplasma pneumoniae, Chlamydophila pneumoniae, and respiratory viruses (eg, influenza, parainfluenza, respiratory syncytial virus) (show figure 2). Legionella pneumoniae and Haemophilus influenzae are less common. The "atypical" pathogens are not often identified in clinical practice because there are not specific, rapid, or standardized tests for their detection, with the exception of L. pneumophila. (See "Clinical manifestations and diagnosis of Legionella infection").

Patients with CAP due to Staphylococcus aureus, Enterobacteriaceae, and Pseudomonas aeruginosa are typically sicker and require admission to the hospital. (See "Treatment of community-acquired pneumonia in adults who require hospitalization" , section on Common

pathogens).

Risk factors for drug resistance — Risk factors for and other issues related to drug resistance in patients with CAP are discussed in detail elsewhere. (See "Antibiotic studies for the treatment of community-acquired pneumonia in adults" , section on Drug resistance and choice of therapy).

Summarized briefly, risk factors for drug-resistant S. pneumoniae in adults include:

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

Recent therapy or a repeated course of therapy with beta-lactams, macrolides, or fluoroquinolones is a risk factor for pneumococcal resistance to the same class of antibiotic.

The impact of discordant drug therapy, which refers to treatment of an infection with an antimicrobial agent to which the causative organism has demonstrated in vitro resistance, appears to vary with antibiotic class and possibly with specific agents within a class. Most studies have been performed in patients with S. pneumoniae infection and suggest that current levels of beta-lactam resistance generally do not cause treatment failure when appropriate agents (eg, amoxicillin , ceftriaxone , cefotaxime) and doses are used. Of the beta-lactams, cefuroxime is a possible exception. In addition, there appears to be an increased risk of macrolide failure in patients with macrolide-resistant S. pneumoniae. (See "Antibiotic studies for the treatment of community-acquired pneumonia in adults" , section on Outcomes with discordant drug therapy).

GUIDELINES — A number of medical societies have issued guidelines for the treatment of CAP [2,9,10] . The antibiotic regimens advocated by a collaboration between the Infectious Disease Society of America and the American Thoracic Society (IDSA/ATS) in 2007 [2] , and guidelines from the British Thoracic Society (BTS) in 2004 [9] are summarized in Table 1 (show table 1). Both guidelines note problems with the emergence of drug-resistant S. pneumoniae (DRSP).

The following discussion will review antibiotic therapy in ambulatory patients with CAP. Guideline recommendations for therapy of patients with CAP treated in the outpatient setting are presented separately. (See "Treatment of community-acquired pneumonia in adults who require hospitalization").

- The regimens chosen by the IDSA/ATS guidelines mainly rely on macrolides (with or without a beta-lactam) or newer fluoroquinolones for outpatient therapy [2] . The guidelines promote the use of macrolides to provide coverage for both S. pneumoniae and atypical pathogens (particularly, M. pneumoniae and C. pneumoniae), which account for the majority of cases of CAP in ambulatory patients (show figure 2). In studies from different regions of the world, atypical pathogens account for 20 to 30 percent of cases of CAP [11] .
- The BTS guidelines tend to select older antibiotics than those recommended in North America [9] .

North American approach — The macrolides, which are effective against the atypical

pathogens, are recommended in the absence of significant risk factors for macrolide-resistant S. pneumoniae. Experience in North America, suggests that macrolide-resistant S. pneumoniae is less significant for patients without comorbidities or risk factors compared to patients with risk factors [8,12,13]. Recent use of macrolide antibiotics is considered a risk factor for resistant S pneumoniae; thus, monotherapy with a macrolide is not recommended for persons who received a macrolide antibiotic in the preceding three months. (See "Resistance of Streptococcus pneumoniae to the macrolides, azalides, lincosamines, and ketolides").

BTS approach — The preferred BTS drug for outpatient management is amoxicillin (500 mg to 1 g orally three times daily), with a macrolide as an alternative for those with penicillin allergy or for "young" patients if Mycoplasma is known to be circulating in the community.

The rationale is that amoxicillin at these doses is effective against most strains of S. pneumoniae with decreased susceptibility to penicillin. Most of the macrolide-resistant S. pneumoniae in Europe is erm-mediated high-level resistance. As a result, the macrolides are not optimal first-line empiric agents. (See "Antibiotic studies for the treatment of community-acquired pneumonia in adults", section on Macrolide resistance, and see "Resistance of Streptococcus pneumoniae to the macrolides, azalides, lincosamines, and ketolides").

Coverage of atypical pathogens — The BTS approach places less significance than the North American approach on the need to treat the atypical pathogens empirically in ambulatory patients. Initial empiric therapy that covers M. pneumoniae is considered unnecessary, since the pathogen exhibits epidemic periodicity every four to five years and largely affects younger persons.

Although the clinical course of M. pneumoniae or C. pneumoniae infection is often self-limited, these pathogens can cause severe CAP. As a result, it has been argued that appropriate treatment for even mild CAP due to Mycoplasma reduces both morbidity and the duration of symptoms [14]. (See "Mycoplasma pneumoniae infection in adults").

The efficacy of empiric coverage of atypical pathogens was evaluated in a 2005 meta-analysis that evaluated 18 randomized trials of over 6700 patients with mild to moderate CAP who were assigned to treatment with either a beta-lactam or an antibiotic active against atypical pathogens [15]. There was no overall advantage to covering atypical pathogens in terms of the rate of failure to achieve clinical cure or improvement (relative risk 0.97, 95% CI 0.87-1.07) but, in a subgroup analysis, there was a significantly lower failure rate for Legionella infection with such a regimen (relative risk 0.40, 95% CI 0.19-0.85). These trials were not designed to compare the time to response with the different regimens.

TREATMENT REGIMENS — Treatment regimens for outpatients with CAP are based upon studies of the effectiveness of antibiotics, the severity of illness, the presence of comorbid conditions, and the prevalence of risk factors for drug resistant S. pneumoniae (DRSP). (See "Antibiotic studies for the treatment of community-acquired pneumonia in adults").

We suggest the following approach to empiric antimicrobial therapy. Pathogen-specific therapy is discussed separately. (See "Pneumococcal pneumonia in adults" and see "Mycoplasma pneumoniae infection in adults" and see "Pneumonia caused by Chlamydophila (Chlamydia) species in adults" and see "Treatment and prevention of Legionella infection" and see "Pseudomonas aeruginosa pneumonia").

No comorbidities or recent antibiotic use — For uncomplicated pneumonia in patients who do not require hospitalization, have no significant comorbidities and/or use of antibiotics within

the last three months, and where there is not a high prevalence of macrolide-resistant strains, we recommend any one of the following oral regimens:

- Azithromycin (500 mg on day one followed by four days of 250 mg a day); 500 mg a day for three days, or 2 g single dose (microsphere formulation) are acceptable alternative regimens
- Clarithromycin XL (two 500 mg tablets once daily) for five days or until afebrile for 48 to 72 hours
- Doxycycline (100 mg twice a day) for seven to 10 days

There is concern that widespread use of fluoroquinolones in outpatients will promote the development of fluoroquinolone-resistance among respiratory pathogens (as well as other colonizing pathogens) and may lead to an increased incidence of C. difficile colitis. In addition, empiric use of fluoroquinolones should not be used for patients at risk for Mycobacterium tuberculosis without an appropriate assessment for tuberculosis infection. The administration of a fluoroquinolone in patients with tuberculosis has been associated with a delay in diagnosis, increase in resistance, and poor outcomes. (See "Antibiotic studies for the treatment of community-acquired pneumonia in adults" , section on Fluoroquinolone resistance, and see "Epidemiology, microbiology, and pathophysiology of Clostridium difficile infection" , section on Antibiotics).

Because of these concerns, the use of fluoroquinolones is discouraged in ambulatory patients with CAP without comorbid conditions or recent antimicrobial use, unless it is known that there is a high prevalence of high-level macrolide-resistant S. pneumoniae in the local community. When such resistance is present, the regimen for patients with comorbidities or recent antibiotic use described in the next section can be followed. (See "Antibiotic studies for the treatment of community-acquired pneumonia in adults" , section on Macrolide resistance).

Despite these recommendations, fluoroquinolones continue to be given, often inappropriately, for CAP. In one report of 768 ambulatory patients with CAP seen in an emergency department in 2000 and 2001, 245 (32 percent) were treated with levofloxacin ; one-half of these patients did not meet the criteria for appropriate fluoroquinolone therapy [7] .

Telithromycin is NOT recommended as a first-line empiric regimen because of concerns about toxicity. (See "Azithromycin, clarithromycin, and telithromycin" , section on Warning about telithromycin).

Although erythromycin is the least expensive macrolide, we rarely use this drug for three reasons: multiple daily doses over several days are required; compliance is limited by gastrointestinal side effects, as well as dosing; and there is a risk of sudden cardiac death due to QT interval prolongation, particularly when other drugs metabolized by CYP3A4 are taken concurrently [16] . The drugs noted above are as effective, more convenient to use, and less toxic. (See "Acquired long QT syndrome").

Comorbidities or recent antibiotic use — The presence of significant comorbidities (ie, chronic obstructive pulmonary disease [COPD], liver or renal disease, cancer, diabetes, chronic heart disease, alcoholism, asplenia, or immunosuppression), and/or use of antibiotics within the prior three months, increases the risk of infection with more resistant pathogens. We recommend one of the following oral regimens for such patients:

- A respiratory fluoroquinolone (gemifloxacin 320 mg daily, levofloxacin 750 mg daily,

or moxifloxacin 400 mg daily) for a minimum of five days. (See "Treatment duration and response" below)

- Combination therapy with a beta-lactam effective against S. pneumoniae (high-dose amoxicillin , 1 g three times daily or amoxicillin-clavulanate 2 g twice daily or cefpodoxime 200 mg twice daily or cefuroxime 500 mg twice daily) PLUS either a macrolide (azithromycin 500 mg on day one followed by four days of 250 mg a day or clarithromycin 250 mg twice daily or clarithromycin XL 1000 mg once daily) or doxycycline (100 mg twice daily). Treatment should be continued for a minimum of five days. (See "Treatment duration and response" below)

These regimens are also appropriate where there is a high prevalence of "high-level" macrolide-resistant S. pneumoniae, even in the absence of comorbidity or recent antimicrobial use. When choosing between fluoroquinolones, in vitro studies of moxifloxacin and gemifloxacin show more activity against penicillin-resistant pneumococci strains than levofloxacin ; the clinical significance of these findings is not yet clear [17] .

Gemifloxacin causes a rash in 2.8 percent of patients overall, but a higher rate (14 percent) in women under 40 years of age who received the drug for seven or more days. The rash is generally mild, occurs after the fifth day of therapy, and resolves with discontinuation of the agent. The rash is not associated with phototoxicity or hypersensitivity and does not preclude the use of other fluoroquinolones in the future, although repeated courses of gemifloxacin should be avoided in such patients. (See "Gemifloxacin: Drug Information").

Telithromycin should be reserved as an option for patients at risk for drug-resistant pneumococcal infection in whom alternative agents are not appropriate. However, it should NOT be prescribed in patients with known liver disease. (See "Azithromycin, clarithromycin, and telithromycin" , section on Warning about telithromycin).

Treatment duration and response — With respect to treatment duration, we generally agree with the 2007 IDSA/ATS guidelines [2] . Ambulatory patients with CAP should be treated for a minimum of five days; because of the prolonged half-life of azithromycin , a shorter duration of drug administration may be indicated for this agent.

Support for this recommendation comes from a meta-analysis of 15 randomized controlled trials of almost 2800 patients with mild to moderate CAP, which found comparable clinical outcomes with less than seven days compared to more than seven days of antimicrobial therapy [18] . Antibiotic therapy should not be stopped until the patient is afebrile for 48 to 72 hours and is clinically stable. (See "Antibiotic studies for the treatment of community-acquired pneumonia in adults" , section on Duration of therapy).

Most patients with CAP begin to improve soon after the initiation of appropriate antibiotic therapy as evidenced by resolution of symptoms, physical findings, and laboratory signs of active infection (show table 2). However, some symptoms often persist as the patient convalesces [19-21] . This was illustrated in a study of sequential interviews in 134 ambulatory patients with CAP [19] . The median time to resolution ranged from three days for fever to 14 days for both cough and fatigue. At least one symptom (eg, cough, fatigue, dyspnea) was still present at 28 days in one-third of patients. In another report, 76 percent had at least one symptom at 30 days, most commonly fatigue, compared to 45 percent by history in the one month prior to the onset of CAP [21] .

These symptoms are usually not sufficient to interfere with work as illustrated in a review of 399 ambulatory patients with CAP in which the median time of return to work was six days even though one-third had at least one persistent symptom at 14 days [20] . (See

"Prognosis of community-acquired pneumonia in adults" , section on Mortality and symptom resolution).

Persistence of such symptoms is not an indication to extend the course of antibiotic therapy as long as the patient has demonstrated some clinical response to treatment [2] .

The nonresponding patient — General issues relating to nonresolving pneumonia are discussed in detail separately. (See "Nonresolving pneumonia"),

Among patients with CAP, nonresponse is primarily seen in those who require hospitalization, occurring in 6 to 15 percent of such patients. The incidence of treatment failure is not well defined in ambulatory patients with CAP because population-based studies would be required [2] . (See "Treatment of community-acquired pneumonia in adults who require hospitalization" , section on The nonresponding patient).

VACCINATION — Patients with CAP should be appropriately vaccinated for influenza and pneumococcal infection. Screening for influenza vaccination status is warranted from October through February in patients age 50 and older or with other indications for vaccination. Screening for pneumococcal vaccination status is warranted in patients age 65 or older or with other indications for vaccination. Vaccination can be performed during outpatient treatment. (See "Influenza vaccination in adults" and see "Pneumococcal vaccination in adults").

SMOKING CESSATION — Smoking cessation should be a goal for patients with CAP who smoke [2] . (See "Management of smoking cessation").

INFORMATION FOR PATIENTS — Educational materials on this topic are available for patients. (See "Patient information: Pneumonia in adults"). We encourage you to print or e-mail this topic review, or to refer patients to our public web site, www.uptodate.com/patients , which includes this and other topics.

SUMMARY AND RECOMMENDATIONS

- Most initial treatment regimens for community-acquired pneumonia (CAP) are empiric. A limited number of pathogens are responsible for the majority of cases of CAP (show figure 1A-1C). (See "Principles of antimicrobial therapy" above).
- Emerging drug-resistant S. pneumoniae (DRSP) complicates the use of empiric treatment. Treatment failures have been demonstrated with use of macrolides for macrolide-resistant organisms. We recommend not prescribing macrolide monotherapy for patients who have received a macrolide antibiotic within the preceding three months (**Grade 1B**).
- Despite in vitro resistance, penicillin-resistant pneumococci may respond to higher dose beta-lactams, other than cefuroxime . Drug toxicity limits the use of telithromycin which should be reserved for patients with "high-level" macrolide-resistant CAP in whom other agents are contraindicated. (See "Risk factors for drug resistance" above).
- North American and British guidelines differ in their recommendations for first-line therapy for outpatient pneumonia. British guidelines promote amoxicillin and place less significance on atypical pathogens. North American guidelines advocate treating both atypical pathogens and pneumococcus, and suggest macrolides when antibiotic resistance is not anticipated. (See "Guidelines" above and see "Coverage of atypical pathogens" above).

- We support the IDSA/ATS guideline recommendations for empiric treatment of CAP in non-hospitalized patients:

- For uncomplicated pneumonia in patients who have no significant comorbidities and/or use of antibiotics within the last three months, we suggest treatment with an advanced macrolide (**Grade 2A**). Regimens include azithromycin (500 mg on day one followed by four days of 250 mg a day, or 500 mg for three days, or 2 g as single dose microsphere regimen) or clarithromycin XL (two 500 mg tablets once daily). We suggest NOT using fluoroquinolones for uncomplicated ambulatory patients with CAP (**Grade 2B**). Alternative regimens are acceptable. (See "No comorbidities or recent antibiotic use" above).

- For non-hospitalized patients with comorbidities or recent antibiotic use, we suggest treatment with a fluoroquinolone as monotherapy, or combination therapy with a beta-lactam plus a macrolide (**Grade 2A**). (See "Comorbidities or recent antibiotic use" above).

- We recommend antibiotic treatment for a minimum of five days, although a shorter duration may be indicated with azithromycin because of its prolonged half-life. Therapy should not be stopped until the patient is afebrile for 48 to 72 hours and is clinically stable. When this is achieved, the persistence of other symptoms (eg, dyspnea, cough) is not an indication to extend the course of antibiotic therapy. (See "Treatment duration and response" above).

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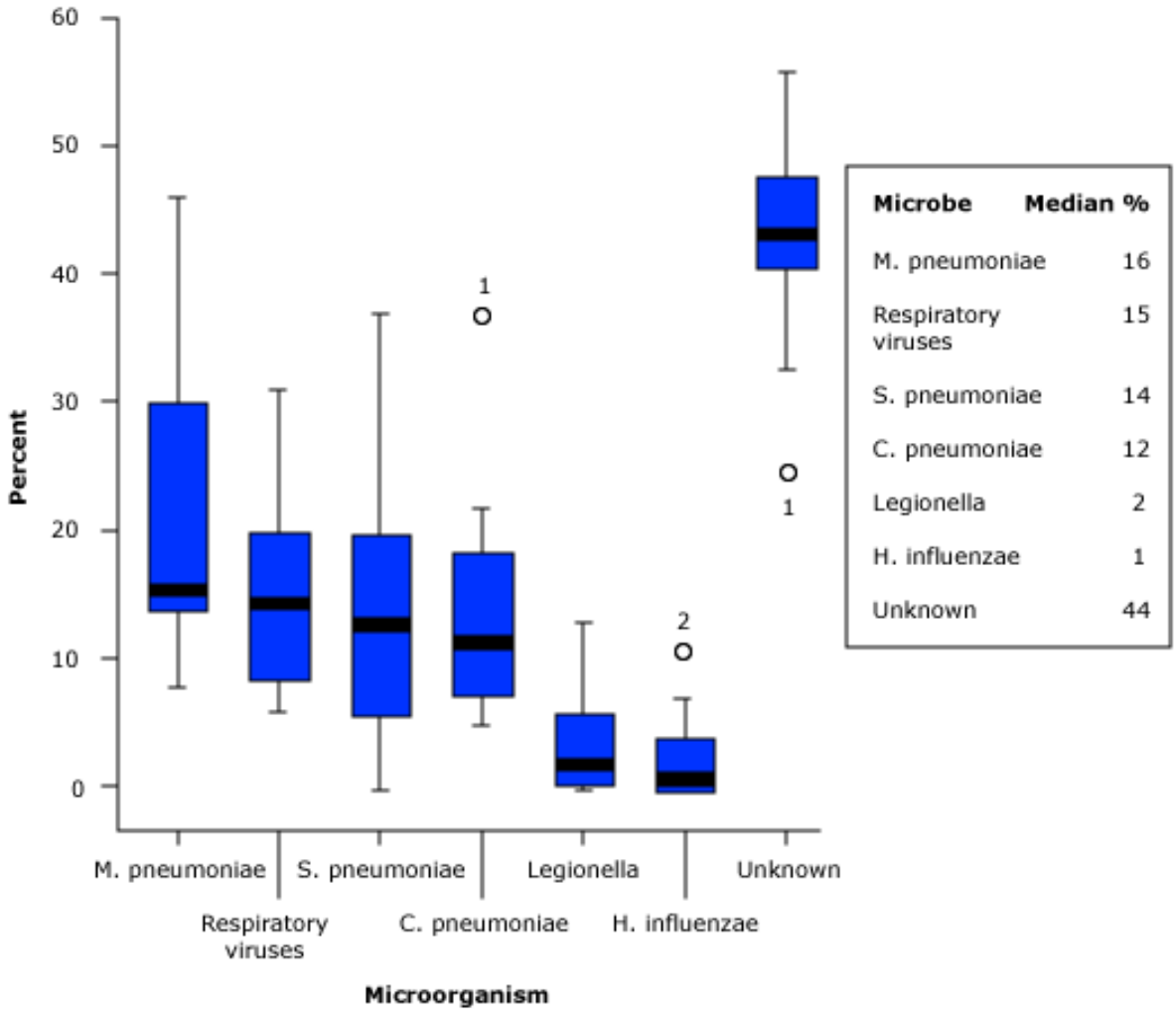
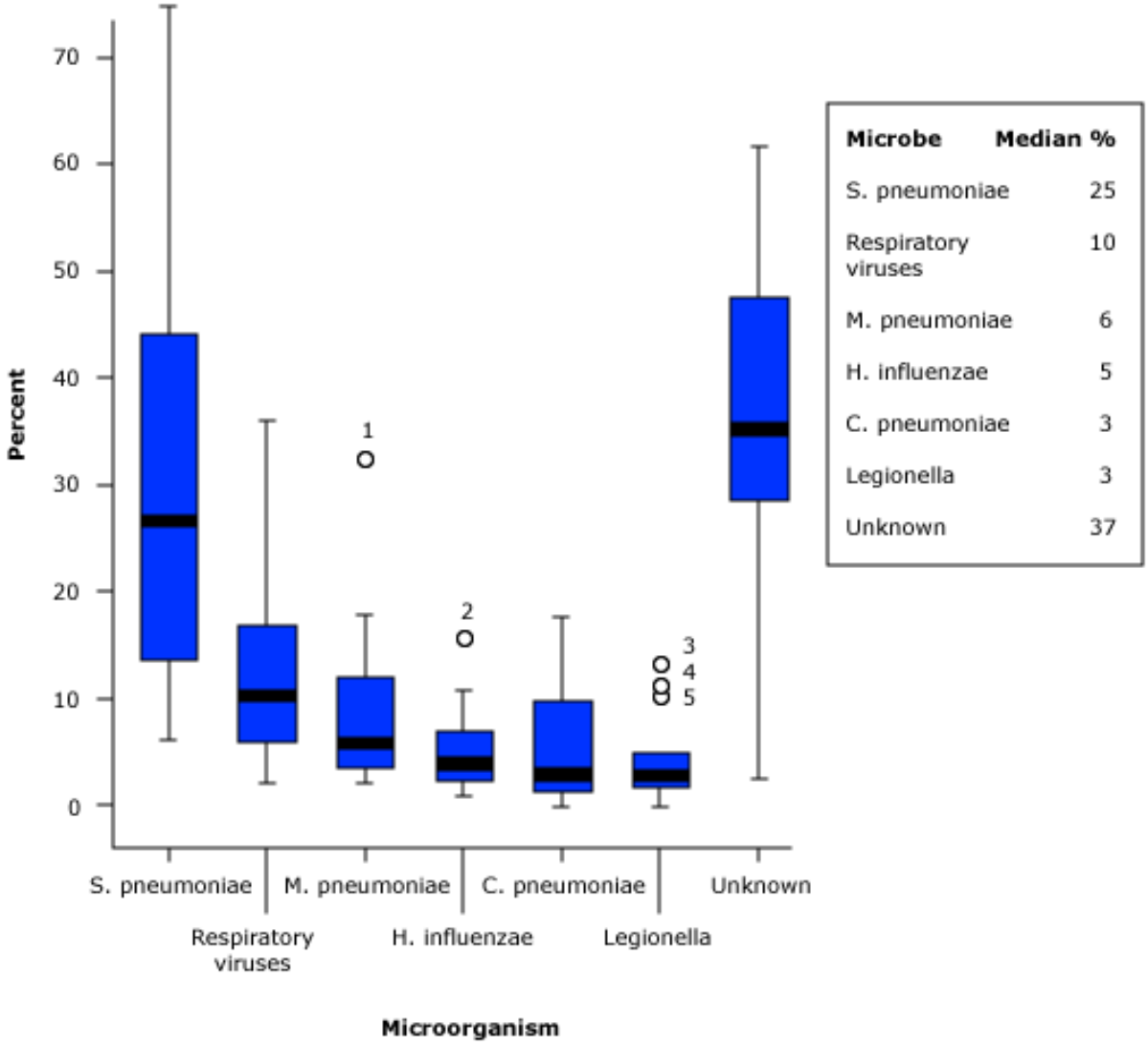
GRAPHICS

Causes of community-acquired pneumonia in ambulatory patients



A box plot depicting the causes of CAP in immunocompetent adults as reported by workers from several studies in worldwide locations whose data could be abstracted by site of care (see text for full references). The bottom and top horizontal lines mark the boundaries of the 5th and 95th percentiles for each microorganism. The box encompasses the 25th through the 75th percentiles. Within the box, the horizontal line represents the median (50th percentile) for each organism. O with number (reference, see below) represents the percent for outlying studies. *1. Chest 2003; 123:1512.*
2. Eur J Clin Microbiol 1986; 5:446.

Causes of community-acquired pneumonia in hospitalized patients (non-ICU)



A box plot depicting the causes of CAP in immunocompetent adults as reported by workers from several studies in worldwide locations whose data could be abstracted by site of care (see text for full references). The bottom and top horizontal lines mark the boundaries of the 5th and 95th percentiles for each microorganism. The box encompasses the 25th through the 75th percentiles. Within the box, the horizontal line represents the median (50th percentile) for each organism. O with number (reference, see below) represents the percent for outlying studies. *1. Arch Intern Med 1997; 157:1709.*

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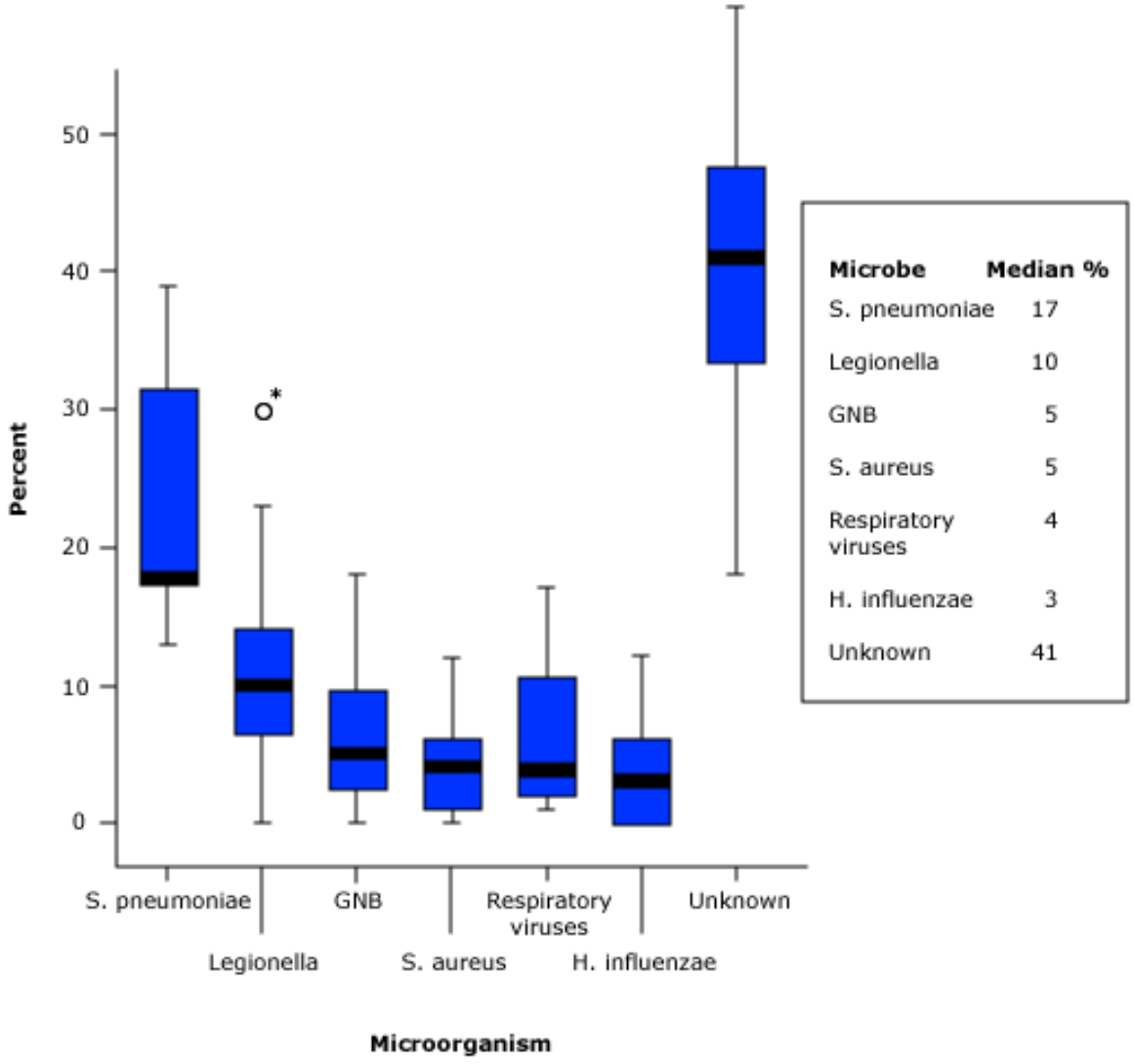
Causes of community-acquired pneumonia in ICU patients (severe CAP)



A box plot depicting the causes of CAP in immunocompetent adults as reported by workers from several studies in worldwide locations whose data could be abstracted by site of care (see text for full references). The bottom and top horizontal lines mark the boundaries of the 5th and 95th percentiles for each microorganism. The box encompasses the 25th through the 75th percentiles. Within the box, the horizontal line represents the median (50th percentile) for each organism. O with number (reference, see below) represents the percent for an outlying study.
GNB: Gram negative bacilli.
** J Infect 1985; 10:204.*

Comparison of recommendations of published guidelines for empiric antimicrobial therapy of community-acquired pneumonia in adults (from North America, United Kingdom)

Guideline	Site of care		
	Outpatient	**General ward**	**ICU/severe**
North American Guideline (ATS/IDSA; 2007) [1]	If no significant risks for DRSP*: Macrolide Δ or doxycycline If risks for DRSP*: Antipneumococcal fluoroquinolone • **OR** High-dose amoxicillin (3 gm/day) or high dose amoxicillin/clavulanate (4 gm/day) **plus** macrolide (if amoxicillin is used and there is a concern for H. influenzae, use macrolide active for β-lactamase producing strains Δ)	β-lactam (ceftriaxone, cefotaxime, ampicillin/sulbactam, ertapenem) **plus** macrolide (can use doxycycline if macrolide not tolerated) **OR** Antipneumococcal fluoroquinolone • alone	β-lactam (ceftriaxone, cefotaxime, ampicillin/sulbactam) **plus** IV azithromycin or IV fluoroquinolone • If concern for Pseudomonas (eg, presence of structural lung disease such as bronchiectasis): antipseudomonal agent (piperacillin/tazobactam, imipenem, meropenem, or cefepime) **plus** antipseudomonal fluoroquinolone (ciprofloxacin or high dose levofloxacin); If concern for MRSA (see text): add vancomycin or linezolid
British Thoracic Society (2004) [2]	Amoxicillin 500-1000 mg thrice daily; (Alternative therapy: erythromycin or clarithromycin)	If admitted for non-clinical reasons or previously untreated in the community: Amoxicillin (macrolide as alternative) If admitted for pneumonia and oral therapy appropriate: Amoxicillin **plus** (erythromycin or clarithromycin); (Alternative therapy: antipneumococcal fluoroquinolone •) If parenteral therapy appropriate: Ampicillin or benzylpenicillin **plus** (erythromycin or	Co-amoxiclav or 2nd/3rd generation cephalosporin **plus** (IV erythromycin or clarithromycin, +/- rifampin); (IV levofloxacin **plus** IV benzylpenicillin as alternative)

		clarithromycin); (Alternative therapy: IV levofloxacin, note IV moxifloxacin not available in UK)	

ICU: intensive care unit; DRSP: drug resistant S. pneumoniae; UK: United Kingdom; IV: intravenous.

* Antimicrobial therapy within the past 3 months, hospitalization within the past month, alcoholism, immune-suppressive illness (including therapy with corticosteroids), multiple medical comorbidities, exposure to a child in a day care center.

• Gemifloxacin, Levofloxacin, Moxifloxacin (Gemifloxacin is only available in oral formulation).

Δ Azithromycin or clarithromycin.

1. Clin Infect Dis. 2007.

2. British Thoracic Society. Pneumonia Guidelines Committee (John MacFarlane, Chair). Guidelines for the management of community-acquired pneumonia-2004 Update. www.Brit-thoracic.org/guideline.

Usual duration of findings in treated community-acquired pneumonia

Abnormality	Duration (days)
Fever	2 to 4
Cough	4 to 9
Crackles	3 to 6
Leukocytosis	3 to 4
C-reactive protein elevation	1 to 3

Grade 1B recommendation

A Grade 1B recommendation is a strong recommendation, and applies to most patients. Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present.

Explanation:

A Grade 1 recommendation is a strong recommendation. It means that we believe that if you follow the recommendation, you will be doing more good than harm for most, if not all of your patients.

Grade B means that the best estimates of the critical benefits and risks come from randomized, controlled trials with important limitations (eg, inconsistent results, methodologic flaws, imprecise results, extrapolation from a different population or setting) or very strong evidence of some other form. Further research (if performed) is likely to have an impact on our confidence in the estimates of benefit and risk, and may change the estimates.

Recommendation grades

1. Strong recommendation: Benefits clearly outweigh the risks and burdens (or vice versa) for most, if not all, patients
2. Weak recommendation: Benefits and risks closely balanced and/or uncertain

Evidence grades

A. High-quality evidence: Consistent evidence from randomized trials, or overwhelming evidence of some other form
B. Moderate-quality evidence: Evidence from randomized trials with important limitations, or very strong evidence of some other form
C. Low-quality evidence: Evidence from observational studies, unsystematic clinical observations, or from randomized trials with serious flaws

For a complete description of our grading system, please see the UpToDate editorial policy which can be found by clicking "About UpToDate" and then selecting "Policies".

Grade 2A recommendation

A Grade 2A recommendation is a weak recommendation, and the best action may differ depending on circumstances or patient or societal values.

Explanation:

A Grade 2 recommendation is a weak recommendation. It means "this is our suggestion, but you may want to think about it." It is unlikely that you should follow the suggested approach in all your patients, and you might reasonably choose an alternative approach. For Grade 2 recommendations, benefits and risks may be finely balanced, or the benefits and risks may be uncertain. In deciding whether to follow a Grade 2 recommendation in an individual patient, you may want to think about your patient's values and preferences or about your patient's risk aversion.

Grade A means that the best estimates of the critical benefits and risks come from consistent data from well-performed, randomized, controlled trials or overwhelming data of some other form (eg, well-executed observational studies with very large treatment effects). Further research is unlikely to have an impact on our confidence in the estimates of benefit and risk.

Recommendation grades
1. Strong recommendation: Benefits clearly outweigh the risks and burdens (or vice versa) for most, if not all, patients
2. Weak recommendation: Benefits and risks closely balanced and/or uncertain

Evidence grades
A. High-quality evidence: Consistent evidence from randomized trials, or overwhelming evidence of some other form
B. Moderate-quality evidence: Evidence from randomized trials with important limitations, or very strong evidence of some other form
C. Low-quality evidence: Evidence from observational studies, unsystematic clinical observations, or from randomized trials with serious flaws

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Grade 2B recommendation

A Grade 2B recommendation is a weak recommendation; alternative approaches may be better for some patients under some circumstances.

Explanation:

A Grade 2 recommendation is a weak recommendation. It means "this is our suggestion, but you may want to think about it." It is unlikely that you should follow the suggested approach in all your patients, and you might reasonably choose an alternative approach. For Grade 2 recommendations, benefits and risks may be finely balanced, or the benefits and risks may be uncertain. In deciding whether to follow a Grade 2 recommendation in an individual patient, you may want to think about your patient's values and preferences or about your patient's risk aversion.

Grade B means that the best estimates of the critical benefits and risks come from randomized, controlled trials with important limitations (eg, inconsistent results, methodologic flaws, imprecise results, extrapolation from a different population or setting) or very strong evidence of some other form. Further research (if performed) is likely to have an impact on our confidence in the estimates of benefit and risk, and may change the estimates.

Recommendation grades
1. Strong recommendation: Benefits clearly outweigh the risks and burdens (or vice versa) for most, if not all, patients
2. Weak recommendation: Benefits and risks closely balanced and/or uncertain

Evidence grades
A. High-quality evidence: Consistent evidence from randomized trials, or overwhelming evidence of some other form
B. Moderate-quality evidence: Evidence from randomized trials with important limitations, or very strong evidence of some other form

C. Low-quality evidence: Evidence from observational studies, unsystematic clinica observations, or from randomized trials with serious flaws

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