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Infectious Diseases: Community-acquired Pneumonia

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Community-acquired pneumonia (CAP) is a common and serious illness. The very young and the very old, smokers and those with cardiopulmonary conditions, alcohol dependence or immunosuppression are at highest risk. While most cases (about 80%) are treated at home, the mortality rate among those requiring hospitalization is 8–10% and up to 40% for those requiring treatment in an intensive care unit (ICU).[1] In general, the clinical presentation of CAP does not allow for an etiologic diagnosis. Many microorganisms cause CAP (Table 1). *Mycobacterium tuberculosis* is an uncommon and often forgotten cause of pneumonia. Consider *M. tuberculosis* particularly in those with pneumonia who are born outside Canada, have HIV or other immune deficiencies and those who are residents of long-term care facilities. Also consider tuberculosis in patients who do not respond to treatment. See Infectious Diseases: Tuberculosis.

Table 1: Pathogens in Community-acquired Pneumonia

Streptococcus pneumoniae *Mycoplasma pneumoniae* *Haemophilus influenzae* *Chlamydophila pneumoniae* *Moraxella catarrhalis* *Legionella* spp. Gram-negative bacilli (e.g., *Escherichia coli*, *Klebsiella* spp., *Enterobacter* spp., *Serratia* spp., *Pseudomonas aeruginosa*)	*Mycobacterium tuberculosis* (uncommon) Respiratory viruses[a] Mixed or polymicrobial etiology (e.g., viral *plus* bacterial) Fungi (uncommon) Aspiration[b]

a. Influenza A and B, adenovirus, parainfluenza, respiratory syncytial virus, human metapneumovirus. Respiratory viruses account for about 15% of CAP cases.[3]

b. Polymicrobial; etiology depends on state of oral hygiene (e.g., periodontal disease—anaerobes; edentulous state—viridans streptococci) and age (aerobic gram-negative bacilli in elderly persons, especially those in long-term care facilities).

Each microbe can result in an illness that spans the spectrum from mild to life-threatening disease. *Streptococcus pneumoniae* accounts for about 50% of all cases of CAP that require hospital admission.[1]

Goals of Therapy

- Assess severity of pneumonia. The pneumonia-specific severity of illness score guides the appropriate location for treatment, i.e., home, hospital ward or ICU (Table 2). Alternatively, consider the functional status of the patient in the week or two prior to admission. For patients who are fully functional, walking with assistance, wheelchair bound and bedridden, the mortality rate is 4%, 5.6%, 20% and 25%, respectively[4]
- Eradicate infecting pathogen
- Relieve symptoms such as cough, pleuritic chest pain, sputum production and/or dyspnea
- Promptly recognize and treat complications such as metastatic infection (meningitis, purulent pericarditis, endocarditis, osteomyelitis), empyema, cavitation, pneumothorax, parapneumonic effusion, septic shock, syndrome of inappropriate antidiuretic hormone (SIADH), delirium, deep vein thrombosis in bedridden patients, respiratory failure and/or worsening of comorbid conditions (ischemic heart disease, diabetes mellitus, COPD)
- Provide compassionate end-of-life care if this emerges

Investigations

- History and physical examination with particular attention to:
  - symptoms: cough, shortness of breath, pleuritic chest pain, hemoptysis, sputum production, fever, chills, myalgia, headache, arthralgia, confusion (new onset may be common in the elderly)
    Check patients with ongoing fever (oral temperature >37.5°C) for empyema. Perform drainage early. Drug fever should be kept in mind and the diagnosis reconsidered if the patient is not improving.
  - history of recent travel and other risk factors for pneumonia such as tobacco smoking, excessive alcohol ingestion, hobbies such as exploring old caves, removal of wild rodent excrement (associated with hantavirus), recent loss of consciousness or comorbid illnesses. Some of these risk factors may influence recovery
  - physical findings: general appearance, e.g., respiratory distress, well or chronically ill or acutely ill. Crackles, wheezes, findings of consolidation of pulmonary tissue (dullness to percussion, increased tactile and vocal fremitus, bronchial breathing, whispered pectoriloquy), pleural friction rub, altered mental status

- Objective measurements:
  - vital signs: respiratory rate ≥30 breaths/minute is the most sensitive and specific sign of severe pneumonia in adults; ≥25 for patients who are <50 years of age
  - oxygenation status: measure oxygen saturation in all patients with CAP presenting to the emergency department. If oxygen saturation <92% in a COPD patient, perform arterial blood gas
  - chest radiograph: posterior-anterior and lateral views. Consider a CT scan of the chest in those who have a negative chest radiograph when pneumonia is clinically suspected

- Laboratory tests for hospitalized patients:
  - electrolytes, glucose, urea, creatinine, CBC and differential white blood cell count
  - consider blood cultures in critically ill patients: 2 samples drawn at separate sites. Anaerobic culture is generally not necessary
  - sputum for Gram stain and culture if a good quality specimen can be obtained. Confirm sputum sample is from the lower respiratory tract (<10 squamous epithelial cells/low-power field). Special requests such as culture for *M. tuberculosis*, Legionella, fungi such as *Blastomyces dermatiditis* or Cryptococcus are dictated by the clinical setting. Consult a microbiologist
  - urine for Legionella antigen if high clinical suspicion for Legionnaires' disease or for patients who require ICU admission because of progressive pneumonia. If available, use polymerase chain reaction test on sputum or other respiratory secretions that can amplify DNA of all Legionella species
  - consider rapid or culture tests for influenza during influenza season
  - consider serologic studies as dictated by clinical setting, e.g., suspected *Mycoplasma pneumoniae* pneumonia. Obtain an acute or a 10- to 14-day convalescent phase serum sample. If Legionnaires' disease is suspected, collect a convalescent phase sample 6 weeks following acute phase serum sample. Hantavirus infection and Q fever (*Coxiella burnetii*) are best diagnosed serologically
  - if a pleural effusion is >1 cm on a decubitus chest film with the affected side down, aspirate and send for pH, culture (aerobes, anaerobes, *M. tuberculosis*), white cell count, LDH and protein. A pH <7.2 suggests the need for prompt drainage to avoid loculation and fibrotic pleural disease
  - for patients admitted to hospital and who undergo bronchoalveolar lavage in addition to routine testing samples, some laboratories have the capacity to use nucleic acid amplification tests to detect nucleic acid of *Legionella* spp., *M. pneumoniae*, Influenza A and B, respiratory syncytial virus, adenovirus, human metapneumovirus, parainfluenza viruses, coronaviruses, rhinoviruses

Therapeutic Choices

Pharmacologic Choices

Successful management of pneumonia (Figure 1 - Initial Management of Community-acquired Pneumonia (CAP)) is based on an accurate assessment of illness severity (Table 2) and selection of the most appropriate site for treatment.[2]

Assessment of Illness Severity

The **Pneumonia-specific Severity of Illness (PSI)** score is designed to predict 30-day mortality rates among patients with CAP and is a validated tool for determining the need for admitting patients to hospital.[5, 6] If the score is **≤90**, treat as outpatient. Some patients in this category may require hospital admission (see Figure 1 - Initial Management of Community-acquired Pneumonia (CAP)). If the PSI score is **≥91**, treat in hospital. However, physician judgment is paramount in the assessment of any patient and should always override any scoring system.

Table 2: Pneumonia-specific Severity of Illness (PSI) Score

Category	Patient Characteristics	Points Assigned
Demographic factors	Male	age (years)
	Female	age (years) minus 10
	Nursing home resident	10
Comorbid illness	Neoplastic disease	30
	Liver disease	20
	Heart failure	10
	Cerebrovascular disease	10
	Renal disease	10
Physical examination findings	Altered mental status	20
	Respiratory rate ≥30 breaths/min	20

Category	Patient Characteristics	Points Assigned
	Systolic blood pressure <90 mm Hg	20
	Temperature <35°C or ≥40°C	15
	Pulse ≥125 beats/min	10
Laboratory findings	Arterial pH <7.35	30
	Blood urea nitrogen >11 mmol/L	20
	Sodium <130 mmol/L	20
	Glucose ≥14 mmol/L	10
	Hematocrit <30%	10
	Partial pressure of arterial oxygen <60 mm Hg	10
	Pleural effusion	10

The CURB-65 tool predicts risk of death and assigns 1 point for each of the following: new onset confusion, urea >7 mmol/L, respiratory rate ≥30 breaths/min, systolic blood pressure <90 mm Hg or diastolic blood pressure ≤60 mm Hg and age ≥65 years. Scores will range from 0.6% (0 points) to 57% (5 points).[7, 8, 9]

SMRT-CO is a tool that accurately predicts which patients with CAP are likely to require intensive respiratory or vasopressor support (IRVS).[10] At initial patient assessment, it measures the systolic blood pressure (<90 mmHg), multilobular chest radiography involvement, respiratory rate (≥25 breaths/minute for those ≤50 years and ≥30 for those >50 years), tachycardia (≥125 bpm), confusion and oxygenation. SMRT-CO scores ≥2, increase the likelihood of the patient requiring IRVS (see Figure 1 - Initial Management of Community-acquired Pneumonia (CAP)). SMART-COP includes the above assessments plus measurements of serum albumin and pH.[10]

Empiric Therapy

Initial empiric antibiotic therapy (Figure 1 - Initial Management of Community-acquired Pneumonia (CAP)) is based on the likely causative pathogen after considering specific risk factors for each patient (e.g., COPD, smoking). Once the etiology is established (Table 3), tailor the antibiotic and/or antifungal therapy paying heed to local susceptibility patterns of bacteria (e.g., *S. pneumoniae*) and local epidemiologic patterns (e.g., outbreaks or endemic foci of Legionella species and dimorphic fungi such as Histoplasma). Antibiotics used in the treatment of CAP are described in Table 4.

Table 3: Antibiotic Therapy for Community-acquired Pneumonia Caused by Specific Pathogens[2]

Organism	Recommended Antibiotics
Streptococcus pneumoniae	**Penicillin nonresistant (MIC <2 mg/L)** *Initial therapy:* penicillin G, amoxicillin. *Alternatives:* macrolide, **po** cephalosporins (cefprozil, cefuroxime), **iv** cephalosporins (cefuroxime, ceftriaxone, cefotaxime), clindamycin, doxycycline, respiratory fluoroquinolones[a] **Penicillin resistant (MIC ≥2 mg/L)** *Initial therapy:* cefotaxime, ceftriaxone, po or iv respiratory fluoroquinolone[a] *Alternatives:* vancomycin, linezolid, high-dose amoxicillin (3 g/day for penicillin MIC ≤4 mg/L)
Haemophilus influenzae	2nd or 3rd generation cephalosporin or amoxicillin/clavulanate, fluoroquinolones, doxycycline, azithromycin, clarithromycin. Amoxicillin monotherapy if non-beta-lactamase producing.
Staphylococcus aureus	Methicillin-susceptible: cloxacillin, cefazolin, clindamycin Methicillin-resistant: vancomycin, linezolid, tigecycline
Legionella species (*Legionnaires' disease*)	Fluoroquinolones or azithromycin, doxycycline (alternative)

Organism	Recommended Antibiotics
Mycoplasma pneumoniae, Chlamydophila pneumoniae	Macrolides or tetracyclines, fluoroquinolones (alternative)
Coxiella burnetii (Q fever)	Doxycycline, fluoroquinolones, macrolides (alternative—although some strains may be resistant)
Aerobic gram-negative bacilli (e.g., *Escherichia coli*, *Enterobacter* spp., *Klebsiella* spp., *Serratia* spp, *Proteus* spp.)	3rd generation cephalosporin, carbapenem[b] (some *Enterobacter* spp. and uncommon strains of *E. coli* and *Klebsiella* spp. produce cephalosporinases and initial therapy should be with piperacillin/tazobactam)
Pseudomonas aeruginosa	Antipseudomonal beta-lactam[c] *plus* ciprofloxacin or aminoglycoside; or aminoglycoside *plus* ciprofloxacin (alternative)

a. Respiratory fluoroquinolones: levofloxacin, moxifloxacin.

b. Carbapenem: ertapenem, imipenem/cilastatin, meropenem.

c. Antipseudomonal beta-lactam: aztreonam, cefepime, ceftazidime, imipenem, meropenem, piperacillin, ticarcillin.

Duration of Antibiotic Therapy

For patients who are well enough to be treated on an ambulatory basis, a minimum of 5 days of antibiotic therapy is required.[2] Patients who are hospitalized and who respond to treatment within 48 hours can be treated with 10 days of antibiotics.[1] Specific etiologies may require longer treatment such as 21 days for severe Legionnaires' disease, 14 days for bacteremic aerobic gram-negative bacilli pneumonia and up to 21 days for pneumonia caused by *Pseudomonas aeruginosa*.[1] Empyema requires drainage and treatment for 14 days or longer. Prolonged therapy is necessary when a lung abscess complicates pneumonia. Antibiotics are given intravenously until the patient has been afebrile for 72 hours and then orally until the cavity has closed, a process that may take 12–16 weeks.

Aspiration Pneumonia

Aspiration pneumonia denotes 2 distinct clinical entities. The first is *aspiration pneumonitis*, which is aspiration of gastric contents (usually sterile as long as there is gastric acid present) into the lungs with a resultant inflammatory response. The second is pneumonia resulting from the aspiration of oropharyngeal flora into the lung with resultant bacterial infection. Risk factors for aspiration include altered level of consciousness, incompetent gastroesophageal junction, elevated intragastric pressure or volume, impaired swallowing mechanisms secondary to neurologic diseases and interference of glottic closure due to neuromuscular diseases.[11]

Generally, younger patients aspirate due to altered level of consciousness (seizures, drugs, alcohol) and older patients aspirate due to neurologic diseases that affect the swallowing mechanism. Patients with aspiration pneumonia require admission to ICU more commonly than those with CAP due to other causes.[12]

Aspiration pneumonitis does not require antibiotic therapy. Patients with aspiration pneumonia who have poor dental hygiene or putrid sputum or who are alcoholics (anaerobic infection suspected), should be treated with **metronidazole**, **clindamycin**, **beta-lactam/beta-lactamase inhibitor** combinations, **carbapenems** and **fluoroquinolones** with established anaerobic activity (e.g., **moxifloxacin**). Treat patients without these specific risk factors for anaerobic infection with standard antibiotics (Figure 1 - Initial Management of Community-acquired Pneumonia (CAP)).

Methicillin-resistant *Staphylococcus aureus* (MRSA) Pneumonia[13]

MRSA, an uncommon yet emerging cause of CAP, accounts for 1–5% of cases. MRSA pneumonia is more common in patients with severe pneumonia who require treatment in an ICU and among residents in long-term care facilities. *S. aureus*, both methicillin-sensitive (MSSA) and MRSA, is about the third most frequent cause of bacteremic pneumonia in the community. *S. aureus* pneumonia has classically been described as a secondary bacterial pathogen in the setting of a primary influenza virus upper respiratory tract infection.[14] , [15] , [16] In the setting of bacteremic *S. aureus* pneumonia, exclude endocarditis (often right sided), especially if multiple rounded opacities are present on the chest radiograph (septic emboli). More recently, community-acquired MRSA infections have been caused by strains producing the Panton-Valentine leukocidin (PVL), known to be associated with tissue necrosis. To date, PVL *S. aureus* infections including pneumonia have been more common in young patients.[17] , [18] **Vancomycin** and **linezolid** are effective choices.[19]

Tigecycline is a glycylcycline, broad-spectrum, intravenous antibiotic that demonstrated noninferiority compared to levofloxacin in clinical trials of CAP.[20] In a murine model of *M. pneumoniae* pneumonia, tigecycline significantly improved lung histologic inflammation and reduced pulmonary cytokines and chemokines.[21] It does have MRSA activity but its role in the treatment of MRSA

pneumonia is still unclear.[22] However, an increase in mortality has been observed when tigecycline was used for certain severe infections including hospital-acquired pneumonia (HAP).[23] , [24] Because of a lack of data, tigecycline is not indicated in severe CAP.

Do not use **daptomycin** in MRSA or any other pneumonia as it is inactivated by pulmonary surfactant.[25]

There is insufficient evidence on which to base firm recommendations for the treatment of severe PVL-producing MRSA pneumonia. In seriously ill patients, consider blocking toxin production by using **clindamycin** in combination with an anti-MRSA agent.

Influenza Pneumonia

The 2009-2010 pandemic of H1N1 (pH1N1) was associated with increased morbidity in younger patients, particularly those aged 20–30 years. Groups at high risk for complications included the morbidly obese, pregnant women, and aboriginal persons.[26] Studies from autopsy specimens of deaths from pH1N1 revealed that bacteria (*S. pneumonia*, Group A Streptococcus, and *S. aureus*) were present in over 55% of cases of which *S. aureus* was a secondary pathogen in 40% and pneumococcus in 35% of cases.[27] , [28]

Current recommendations for treatment of Influenza A or B virus infection include the neuramidase inhibitors **oseltamivir** and **zanamivir**.[29] **Amantadine** is no longer recommended because of viral resistance (see Infectious Diseases: Influenza). The appropriate treatment will vary from year to year depending on the susceptibilities of the season's circulating strains. Unlike uncomplicated influenza, treatment may be initiated in hospitalized patients with influenza pneumonia even after 48 hours of the onset of symptoms.[2] The major concern is bacterial superinfection and this has to be treated immediately.

Prevention of Community-acquired Pneumonia

Smoking Cessation

Encourage smoking cessation (see Psychiatric Disorders: Smoking Cessation). Tobacco smoking is associated with a two-fold increase in risk for invasive pneumococcal pneumonia.[30] It is likely that cessation of tobacco smoking will reduce the rate of pneumonia, but there are no data from clinical trials. Nevertheless, this recommendation is likely to have many benefits, including slowing the age-related decline in lung function and reducing the risk of lung cancer.

Vaccines

Influenza Vaccine

Annual influenza vaccination is recommended for those at high risk of complications from influenza and anyone >6 months who wants to avoid developing influenza.[31] Previous studies have reported that immunization of the elderly reduces the rate of admission to hospital for both pneumonia and heart failure;[32] hospitalized patients with CAP demonstrated improved survival from prior vaccination;[33] and immunization of health care workers against influenza reduces the mortality rate due to influenza in patients.[34] Although these studies demonstrated benefit, later evidence suggested that the beneficial effects of influenza vaccine may have been overestimated because of a "healthy user effect"; a 51% reduction in mortality with influenza vaccination was observed in patients who developed CAP outside the influenza season.[35] Until newer vaccine formulations are introduced and proven to be effective (e.g., higher dosages) current recommendations should be followed. Cluster randomized trial data suggest that immunizing healthcare workers reduces morbidity and mortality in patients,[36] , [37] , [38] , [39] although a Cochrane review concluded otherwise.[40] See Infectious Diseases: Influenza.

Pneumococcal Vaccine

Two types of pneumococcal vaccines are available in Canada—polysaccharide and conjugate (polysaccharide conjugated to a protein carrier to enhance immunogenicity). A 23-valent capsular **polysaccharide vaccine (PNEU-P-23)** contains the most common capsular polysaccharide types of *S. pneumoniae* that cause bacteremic pneumonia.[41] While evidence of effectiveness has been mixed, a Cochrane review showed that pneumococcal polysaccharide vaccines are effective in preventing pneumococcal bacteremia and pneumococcal pneumonia; however, the evidence for preventing all-cause pneumonia is weak.[42] In patients admitted to hospital with CAP, prior PNEU-P-23 vaccination reduced mortality and ICU admission.[43]

Conjugate pneumococcal vaccines are used in the routine immunization of children, which has resulted in a reduction in but not elimination of invasive pneumococcal disease among adults because of herd immunity.[44] A 13-valent polysaccharide-protein conjugate vaccine (PNEU-C-13) is approved for adults ≥50 years of age though there is no

clear evidence that it is more effective than PNEU-P-23.[45] However, based on improved immunogenicity over PNEU-P-23 seen in some studies and an increased risk of invasive pneumococcal disease in immunocompromised persons, Canadian recommendations are to provide PNEU-C-13 to immunocompromised adults, followed by immunization with PNEU-P-23 [SORT C].[45] Useful Info? See Table 5 for indications and schedules for the recommended pneumococcal vaccines.

Prevention of Aspiration Pneumonia

For patients at risk of aspiration, the "chin down" posture may reduce the occurrence of aspiration both before and during the swallow, however definitive evidence is lacking.[46] This posture results in a posterior shift of the anterior pharyngeal structures, narrowing the laryngeal entrance while widening the angle of the epiglottis to the anterior tracheal wall. The end result is protection of the airway. Cleaning of the teeth and gingiva by caregivers after each meal reduced the latency time of the swallowing reflex and increased substance P in the saliva of patients with dysphagia due to cerebrovascular disease.[47] Substance P stimulates the neural pathways to improve the swallowing reflex. Elevation of the head of the bed is also helpful in preventing aspiration pneumonia.

Choices during Pregnancy and Breastfeeding

Community-acquired Pneumonia (CAP) and Pregnancy

CAP in pregnancy is not uncommon, accounting for about 4% of antepartum hospitalizations for nonobstetric complications.[48] It is believed that CAP poses a disproportionate burden of illness in pregnant women and should be promptly diagnosed and treated.[49] If left untreated, pneumonia in pregnancy can cause life-threatening disease to the mother and adverse effects to the infant (e.g., preterm birth, low birth weight).

Management of CAP in Pregnant Women

Clinical presentation of CAP is similar to nonpregnant patients. Perform a chest radiograph in patients for whom CAP is suspected. In healthy pregnant women with no recent antibiotic exposure, use of **azithromycin** or **erythromycin** (except the estolate salt) is recommended.[2] One small study (n=122) suggests a possible increased risk of spontaneous abortion with the use of **clarithromycin**, but this has not been confirmed with additional studies and may have been due to confounding factors.[50] Treat women with severe CAP with a **beta-lactam** and **macrolide**.[2] **Amoxicillin** or **amoxicillin/clavulanate** are preferred beta-lactams; alternatives include **ceftriaxone** and **cefuroxime**. Ideally, local macrolide and beta-lactam resistance rates should be available to tailor the regimen. In settings with high beta-lactam and macrolide resistance, **fluoroquinolones** are preferred; their risk of teratogenicity is low. If community-acquired MRSA is suspected, add **vancomycin** to the chosen regimen. If *Pseudomonas* is isolated, use an antipseudomonal beta-lactam such as **piperacillin/tazobactam** or **cefepime** plus an **aminoglycoside** and **azithromycin**.[2] In most women there will be clinical improvement within 48–72 hours, and therapy should not be changed in the first 72 hours unless there is marked clinical deterioration.[49] Fever should resolve in 2–4 days and cough after 7–10 days. Radiologic abnormalities may persist for up to 6 weeks, so continued hospitalization is not required to await radiologic improvement. Therapy is recommended for a minimum of 5 days for uncomplicated CAP. Treatment failures may be encountered in up to 15% of cases; choose a broad-spectrum regimen or more specific treatment if the infecting agent is identified.

Management of CAP in Breastfeeding Women

The antimicrobials recommended in pregnancy (above), including those for MRSA, are considered compatible with breastfeeding.[51], [52]

Prevention of CAP in Pregnant and Breastfeeding Women

Pregnant women should be immunized against influenza because of the high risk for complications. Pneumococcal 23-valent polysaccharide conjugate vaccine is recommended for pregnant women with conditions placing them at higher risk of pneumococcal disease, i.e., immunosuppression, cigarette smoking, alcoholism, diabetes, cardiac, pulmonary or renal disease or asplenia (e.g., sickle-cell disease). Primary prevention strategies such as handwashing and limiting contact with sick individuals reduce the risk of respiratory infections.

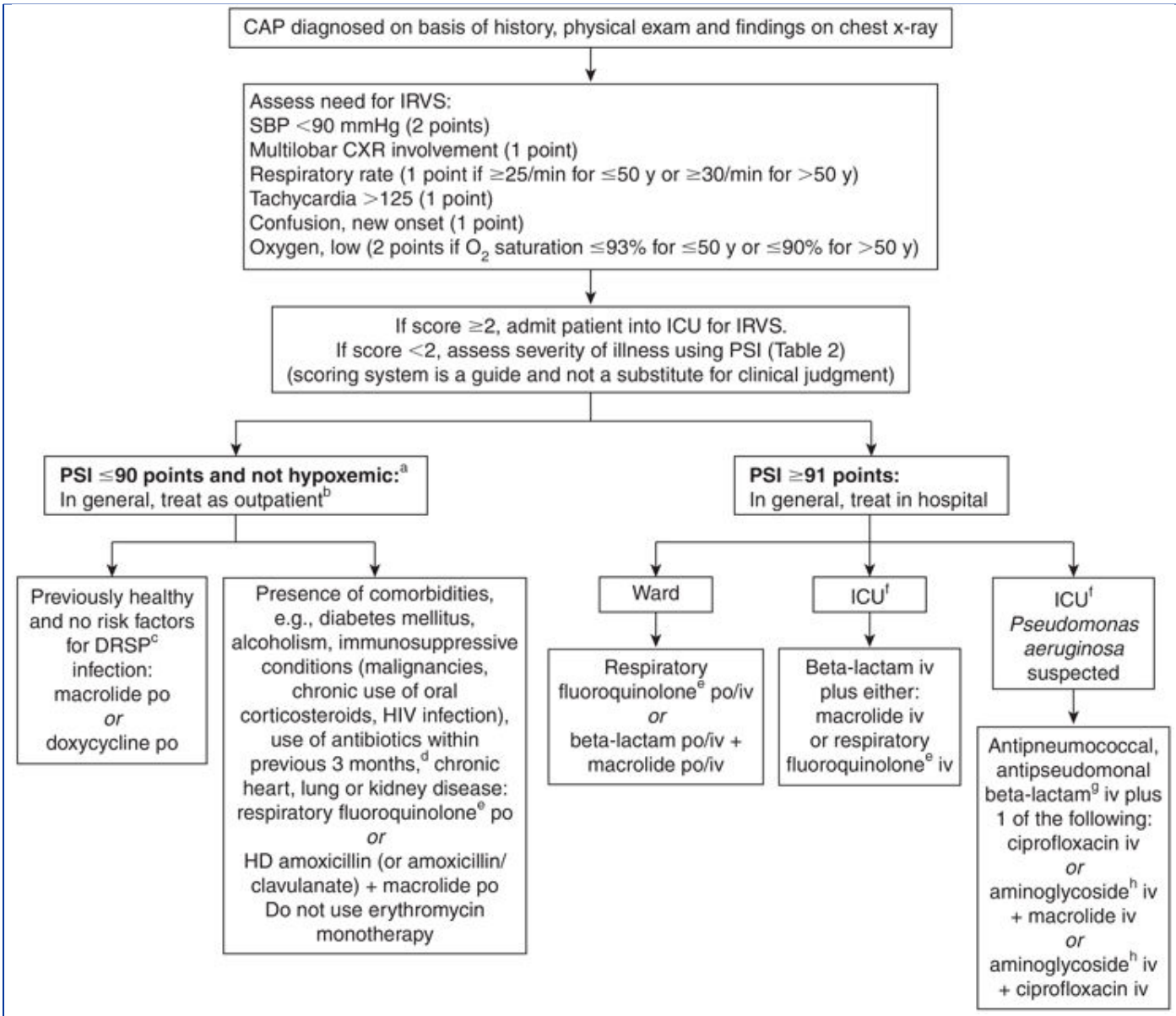
A discussion of general principles on the use of medications in these special populations can be found in Drug Use During Pregnancy and Drug Use During Breastfeeding. Other specialized reference sources are also provided in these appendices.

Therapeutic Tips

- Administer an agent from a different therapeutic class if the patient has received antibiotics within the 3 months prior to diagnosis of CAP.
- Because of its lowered activity against *H. influenzae*, **erythromycin** *monotherapy* is not routinely recommended in patients with COPD.
- In the outpatient setting, the superiority of one agent over another is difficult to define because most of the randomized, controlled trials are noninferiority studies conducted for licensing purposes. Despite the recommendation from various guidelines for empiric coverage of atypical pathogens in hospitalized patients, there is no evidence that regimens which include atypical coverage result in better outcomes than those that do not.[53]
- Switch patients from intravenous to oral antibiotics when the following criteria are met:[2], [54], [55] GI tract is functioning normally (e.g., no vomiting, diarrhea or disorder compromising GI absorption); hemodynamically stable; 2 temperature readings are normal (oral temperature <37.5°C) over a period of 16 hours in previously febrile patients; normalized white blood cell count; subjective improvement in cough and shortness of breath; able to consume oral medications. If blood cultures are positive, the duration of intravenous therapy is dictated by the organism recovered from the blood. Use of clinical pathways that emphasize early antibiotic switch and early mobilization may reduce lengths of hospital stay.[56]
- Discharge the patient when the following criteria are met in addition to those above: absence of complications from the pneumonia (e.g., empyema); absence of complications from comorbid illnesses (e.g., MI); absence of complications from treatment (e.g., severe adverse drug reactions); physiological stability as indicated by an oxygen saturation of ≥92% while breathing room air for those who do not have COPD (for patients with COPD, a return to baseline status is desirable), pulse rate of <100 beats/minute and respiratory rate ≤24 breaths/minute.[2]
- Evidence from one randomized, controlled trial suggests that early mobilization during management of CAP can reduce length of stay.[57]
- Prevent recurrent pneumonia in patients ≥65 years and in those suffering from recurrent episodes. A checklist that includes identification of causes of aspiration and measures to prevent recurrent aspiration may be useful.
- Review pneumococcal and influenza vaccine status and immunize if indicated.
- Consider follow-up chest radiographs for *all patients over age 50*, particularly if a smoker. One to two per cent of all patients with CAP will have lung cancer and in half of these the cancer is not diagnosed on the initial radiograph.[58], [59] Do the follow-up chest radiograph 6–12 weeks after presentation. If the pneumonic opacity is still present, further investigation such as bronchoscopy may be warranted.

Algorithm

Figure 1 - Initial Management of Community-acquired Pneumonia (CAP)



a. Approximately 20% of patients in this category will require admission.[1]

b. Psychosocial and medical factors, e.g., can reliably take oral medications, exacerbation of underlying disease (diabetes, COPD, heart failure), homelessness, may influence the decision to admit.

c. Risk factors for DRSP include age <2 or >65 years, comorbid conditions, antibiotic use in the previous 3 months, alcoholism, immunosuppressive conditions and exposure to a child in a daycare centre.[2]

d. For patients who have received an antibiotic within the past 3 months, use another class of antibiotics.

e. Respiratory fluoroquinolone: levofloxacin, moxifloxacin. For hospitalized patients, the dose of levofloxacin is 750 mg once daily for 5 days.

f. Absolute indications for admittance into ICU: a) septic shock requiring vasopressors; b) acute respiratory failure requiring endotracheal intubation and mechanical ventilation.

g. Cefepime, imipenem, meropenem, piperacillin/tazobactam.

h. For patients who have received a fluoroquinolone within the past 3 months choose an aminoglycoside-containing regimen.

Abbreviations: CXR=chest x-ray; DRSP=drug-resistant S. pneumoniae ; HD=high-dose; ICU=intensive care unit; IRVS=intensive respiratory or vasopressor support; PSI=pneumonia-specific severity of illness

Drug Tables

Table 4: Anti-infectives for the Treatment of Pneumonia

Drug Class	Drug	Dose	Adverse Effects	Comments	Cost[a]
Aminoglycosides	*gentamicin* generics	Conventional dosing: 1.5 mg/kg DBW[b] Q8H iv Extended-interval dosing: 4–7 mg/kg DBW[b] once daily iv	Nephrotoxicity, ototoxicity.	Aminoglycosides do not penetrate pulmonary tissue very well. Exhibits concentration-dependent bacterial killing and postantibiotic effect. Coadministration of vancomycin or loop diuretics may increase risk of nephrotoxicity and ototoxicity, respectively. Coadministration of penicillins in vivo or in iv bags and syringes may result in aminoglycoside inactivation.	$
Aminoglycosides	*tobramycin* generics	Conventional dosing: 1.5 mg/kg DBW[b] Q8H iv Extended-interval dosing: 4–7 mg/kg DBW[b] once daily iv	Nephrotoxicity, ototoxicity.	Aminoglycosides do not penetrate pulmonary tissue very well. Exhibits concentration-dependent bacterial killing and postantibiotic effect. Coadministration of vancomycin or loop diuretics may increase risk of nephrotoxicity and ototoxicity, respectively. Coadministration of penicillins in vivo or in iv bags and syringes may result in aminoglycoside inactivation.	$
Carbapenems	*ertapenem* Invanz	1 g daily iv	Anaphylaxis, increased seizure risk (compromised renal function, CNS disorders, e.g., history of seizures), diarrhea, headache.	Indicated for *S. pneumoniae* (penicillin-susceptible strain only), *H. influenzae* (beta-lactamase negative strain only) or *M. catarrhalis*.	$$
Carbapenems	*imipenem/cilastatin* Primaxin, generics	500 mg Q6H iv	Hypotension, nausea with rapid infusion; seizure activity with high serum levels.	Antipseudomonal. For patients with risk factors for *P. aeruginosa*.	$$$
Carbapenems	*meropenem* Merrem, generics	1 g Q8H iv	Hypotension, nausea with rapid infusion; less likely than imipenem to cause seizures.	Antipseudomonal. For patients with risk factors for *P. aeruginosa*.	$$$$
Cephalosporins, first-generation	*cefazolin* generics	1– 2 g Q8H iv	Anaphylaxis, rash, gastrointestinal upset, renal and hepatic dysfunction, phlebitis at site of injection.	Alternative choice in methicillin-sensitive *S. aureus* pneumonia.	$
Cephalosporins, second-generation	*cefaclor* Ceclor, generics	250 mg TID po	Anaphylaxis, rash, gastrointestinal upset, renal and hepatic dysfunction.		$

Drug Class	Drug	Dose	Adverse Effects	Comments	Cost[a]
Cephalosporins, second-generation	*cefprozil* Cefzil, generics	500 mg BID po	Anaphylaxis, rash, gastrointestinal upset, renal and hepatic dysfunction.		$
Cephalosporins, second-generation	*cefuroxime axetil* Ceftin, generics	500 mg BID po	Anaphylaxis, rash, gastrointestinal upset, renal and hepatic dysfunction.	Do not use for treatment of penicillin-resistant *S. pneumoniae* .	$
Cephalosporins, second-generation	*cefuroxime sodium* generics	750 mg Q8H iv	Anaphylaxis, rash, gastrointestinal upset, renal and hepatic dysfunction, phlebitis at site of injection.	Do not use for treatment of penicillin-resistant *S. pneumoniae* .	$$
Cephalosporins, third-generation	*cefotaxime* Claforan	1–2 g Q8H iv	Anaphylaxis, rash, gastrointestinal upset, renal and hepatic dysfunction, phlebitis at site of injection.	Can be used in hepatobiliary disease.	$$
Cephalosporins, third-generation	*ceftazidime* Fortaz, generics	1–2 g Q8H iv	Anaphylaxis, rash, gastrointestinal upset, renal and hepatic dysfunction, phlebitis at site of injection.		$$$-$$$$
Cephalosporins, third-generation	*ceftriaxone* generics	1–2 g Q24H iv	Anaphylaxis, rash, gastrointestinal upset, renal and hepatic dysfunction, phlebitis at site of injection.	Do not reconstitute or mix with calcium-containing solutions. Do not administer simultaneously with calcium-containing iv solutions via a Y-site. Administration may be done sequentially provided the infusion lines are thoroughly flushed between infusions.	$
Cephalosporins, fourth-generation	*cefepime* Maxipime, generics	1– 2 g Q12H iv	Anaphylaxis, rash, gastrointestinal upset, renal and hepatic dysfunction, phlebitis at site of injection. Risk of seizures particularly in those with renal dysfunction.	Antipseudomonal; for patients with risk factors for *P. aeruginosa*.	$$
Fluoroquinolones	*ciprofloxacin* Cipro, generics	Oral: 500– 750 mg BID IV: 400 mg Q12H	Gastrointestinal upset, headache, dizziness, photosensitivity, hepatitis. Cartilage toxicity: *avoid in children*.	Ciprofloxacin is *not* a first-line agent for CAP. Available as an oral suspension. Incidence of ciprofloxacin-resistant (MIC ≥4 mg/L) *S. pneumoniae* isolates in Canada in 2012 was 2.2%.[60] Concomitant antacids, metal cations, sucralfate decrease absorption of fluoroquinolones. Ciprofloxacin may decrease theophylline or	Oral: $ IV: $$

Drug Class	Drug	Dose	Adverse Effects	Comments	Cost[a]
				cyclosporine elimination; may prolong the INR if given with warfarin.	
Fluoroquinolones	*levofloxacin* Levaquin, generics	Oral: 500 mg Q24H × 10 days *or* 750 mg Q24H × 5 days IV: 500 mg once daily	Gastrointestinal upset, headache, dizziness, photosensitivity, hepatitis. Cartilage toxicity: *avoid in children*.	Levofloxacin 750 mg daily for 5 days is equivalent to 500 mg daily for 10 days.[61] An alternative to β-lactam/macrolide combination for patients on hospital wards. Can switch from iv to po therapy while maintaining serum levels. Concomitant antacids, metal cations, sucralfate decrease absorption of fluoroquinolones. May increase warfarin effect. Avoid in patients on Class Ia or III antiarrhythmics or with prolonged QT_C interval. Cases of severe liver injury including liver failure have been reported.	Oral: $ IV: $$
Fluoroquinolones	*moxifloxacin* Avelox	400 mg Q24H po/iv	Gastrointestinal upset, headache, dizziness, photosensitivity, hepatitis. Cartilage toxicity: *avoid in children*.	An alternative to beta-lactam/macrolide combination for patients on hospital wards. Can switch from iv to po therapy while maintaining serum levels. Concomitant antacids, metal cations, sucralfate decrease absorption of fluoroquinolones. Avoid in patients on Class Ia or III antiarrhythmics or with prolonged QT_C interval. Cases of severe liver injury including liver failure have been reported.	Oral: $ IV: $$
Glycopeptides	*vancomycin* generics	1 g Q12H iv	Infusion-related adverse effects occur with shorter infusion times: intense flushing (red man or red neck syndrome),	For MRSA-pneumonia. Coadministration with aminoglycosides may increase risk of nephrotoxicity.	$$$$

Drug Class	Drug	Dose	Adverse Effects	Comments	Cost[a]
			hypotension. Nephrotoxicity, ototoxicity.		
Glycylcyclines	*tigecycline* Tygacil	100 mg iv then 50 mg Q12H	Nausea, vomiting, diarrhea, acute pancreatitis (rare).	Contraindicated if hypersensitivity with tetracyclines as it is structurally related. Not indicated for severe CAP or hospital-acquired pneumonia (HAP). Lower cure rates and higher mortality have been seen when used for HAP.	$$$$$
Lincosamides	*clindamycin* Dalacin C, Dalacin C Flavored Granules, Dalacin C Phosphate Solution Sterile, generics	Oral: 300–450 mg Q6H IV: 600 mg Q8H	Abdominal pain, nausea, vomiting, diarrhea, *C. difficile* colitis.	Incidence of clindamycin-resistant *S. pneumoniae* isolates in Canada in 2012 was 9.6%.[60] For suspected aspiration; provides oral anaerobic coverage.	$
Macrolides	*azithromycin* Z-PAK, Zithromax, Zmax SR , generics	Oral: 500 mg 1st day then 250 mg × 4 days *or* 500 mg daily × 3 days IV: 500 mg daily × 7– 10 days Zmax SR: 2 g po once; indicated for mild CAP only	Better tolerated than erythromycin. Gastrointestinal upset, rash, cholestatic hepatitis, QT_C interval prolongation.	Oral azithromycin given daily × 5 days is equivalent to oral erythromycin QID × 10 days. A 5-day course of azithromycin is adequate for mild to moderate CAP. Azithromycin more active than clarithromycin for *H. influenzae*. Use cautiously with other drugs that cause QT_C prolongation.	$
Macrolides	*clarithromycin* Biaxin, Biaxin XL, generics	Regular-release: 500 mg BID po Extended-release: 1000 mg once daily po	Better tolerated than erythromycin. Gastrointestinal upset, rash, cholestatic hepatitis, QT_C interval prolongation. May increase the risk of cardiovascular events that last beyond the period of clarithromycin therapy.[62]	Coadministration with pimozide is contraindicated. Rifampin: decreased macrolide concentrations. May increase warfarin effect; increased concentrations of substrates of CYP3A4 (potent inhibitor), e.g., atorvastatin, carbamazepine, digoxin, lovastatin, simvastatin. Use cautiously with other drugs that cause QT_C prolongation.	$

Drug Class	Drug	Dose	Adverse Effects	Comments	Cost[a]
Macrolides	*erythromycin* Eryc, generics	500 mg QID po	Gastrointestinal upset, rash, cholestatic hepatitis, QT_C interval prolongation.	Coadministration with pimozide is contraindicated. Rifampin: decreased macrolide concentrations. May increase warfarin effect; increased concentrations of substrates of CYP3A4 (potent inhibitor), e.g., atorvastatin, carbamazepine, digoxin, lovastatin, simvastatin. Use cautiously with other drugs that cause QT_C prolongation.	$
Nitroimidazoles	*metronidazole* Flagyl, generics	500 mgQ8H po/iv	Vertigo, headache, ataxia, gastrointestinal upset, taste alterations.	For suspected aspiration pneumonia; provides anaerobic coverage. Not to be used as monotherapy. Concomitant intake of ethanol may lead to a disulfiram-like reaction; avoid alcohol for at least 24 h after last dose of metronidazole.	$
Oxazolidinones	*linezolid* Zyvoxam	600 mg Q12H po/iv	Gastrointestinal upset, headache, dose- and time-dependent bone marrow suppression, peripheral neuropathy, optic neuritis (rare).	Suitable choice for MRSA-pneumonia.[19, 63] Monitor complete blood count at least weekly for myelosuppression particularly if given for over 2 wk. Increased risk of serotonin toxicity with concomitant serotonergic drugs, e.g., selective serotonin reuptake inhibitors.[64, 65]	$$$$$
Penicillins	*penicillin V potassium* generics	300 mg TID-QID po	Hypersensitivity reactions, rash, gastrointestinal upset, interstitial nephritis.		$
Penicillins	*penicillin G* Crystapen, generics	2 million U Q4H iv	Hypersensitivity reactions, rash, gastrointestinal upset, interstitial nephritis.		$
Penicillins	*amoxicillin* generics	500 mg TID po High-dose: 1 g TID po	Hypersensitivity reactions, rash, gastrointestinal upset, interstitial nephritis.	Consider high-dose amoxicillin if patient presents with drug-resistant *S. pneumoniae* risk factors.	$
Penicillins	*amoxicillin/clavulanate* Clavulin, generics	500/125 mg TID *or* 875/ 125 mg BID po	Hypersensitivity reactions, rash, gastrointestinal upset,	Consider high-dose amoxicillin/clavulanate if patient presents with	$

Drug Class	Drug	Dose	Adverse Effects	Comments	Cost[a]
			interstitial nephritis.	drug-resistant *S. pneumoniae* risk factors.	
Penicillins	*ampicillin* generics	1 g Q6H iv	Hypersensitivity reactions, rash, gastrointestinal upset, interstitial nephritis.		$
Penicillins	*cloxacillin* generics	1–2 g Q6H iv	Hypersensitivity reactions, rash, gastrointestinal upset, interstitial nephritis.		$
Penicillins	*piperacillin* generics	3 g Q4H iv *or* 4 g Q6H iv	Hypersensitivity reactions, rash, gastrointestinal upset, interstitial nephritis.		$$$
Penicillins	*piperacillin/tazobactam* Tazocin, Piperacillin/Tazobactam for Injection, other generics	3 g/0.375 g Q6H iv	Hypersensitivity reactions, rash, gastrointestinal upset, interstitial nephritis.	Antipseudomonal; for patients with risk factors for *P. aeruginosa*.	$$$
Penicillins	*ticarcillin/clavulanate* Timentin	>60 kg: 3.1 g Q4–6H iv <60 kg: 200–300 mg/kg/day divided Q4–6H iv	Hypersensitivity, gastrointestinal upset.		$$
Rifamycins	*rifampin* Rifadin, Rofact	300 mg BID po	Rash (petechial rash may suggest thrombocytopenia), orange discolouration of body fluids (contact lens staining), GI upset, liver toxicity, hematologic effects (e.g., thrombocytopenia).	*Should never be used as a single agent for CAP.* May be used as adjunctive therapy in *Legionella* or *S. aureus* pneumonia. Induction of CYP isozymes resulting in many potential interactions (e.g., may decrease levels of cyclosporine, tacrolimus, sirolimus, phenytoin, warfarin and oral contraceptives). Adjust dose of affected drug when rifampin is initiated or discontinued.	$
Tetracyclines	*doxycycline* Vibramycin, generics	100 mg BID po 1st day then 100 mg daily	Gastrointestinal upset, photosensitivity.	Iron or antacids may decrease doxycycline absorption. Alcohol, barbiturates, phenytoin, rifampin, carbamazepine may decrease doxycycline levels.	$
Antivirals	*oseltamivir* Tamiflu	75 mg BID po × 5 days	Nausea, vomiting, headache.		$

Drug Class	Drug	Dose	Adverse Effects	Comments	Cost[a]
Antivirals	*zanamivir* Relenza	10 mg (2 inhalations) BID × 5 days	Bronchospasm has been reported, especially in patients with respiratory disease. Headache, dizziness, cough.	Do not use in patients with asthma or COPD due to risk of serious bronchospasm.	$$

a. Cost of oral and iv medications is per 1-day supply based on 6-foot male; cost of inhaled agents is per unit; includes drug cost only.

b. In obese patients (>30% ideal body weight [IBW]), use dosing body weight (DBW) instead of total body weight (TBW) to prevent overdosing. DBW = IBW + 0.4(TBW-IBW) where IBW (kg; males) = 50 + (2.3 × height in inches over 5 feet). IBW (kg; females) = 45.5 + (2.3 × height in inches over 5 feet).

Dosage adjustment may be required in renal impairment; see Appendices: Dosage Adjustment in Renal Impairment.

Legend: $ < $25 $$ $25–50 $$$ $50–100 $$$-$$$$ $50–150 $$$$ $100–150 $$$$$ $150–200

Table 5: Pneumococcal Vaccines for Preventing Community-acquired Pneumonia

Class	Vaccine	Indications	Dose[41]	Comments	Cost[a]
Pneumococcal vaccines, conjugate	*pneumococcal 13-valent conjugate vaccine (PNEU-C-13)* Prevnar 13	Routine infant immunization	For dose schedule in children, see Table 3 in Infectious Diseases: Acute Otitis Media in Childhood		$95
		Adult hematopoietic stem cell transplant (HSCT) recipients	3 doses (0.5 mL/dose) im administered 4 wk apart, starting 3–9 months after transplant	Persons who are eligible for both conjugate and polysaccharide vaccines should receive conjugate vaccine first. However, those who have already received PNEU-P-23 may still receive PNEU-C-13, in which case administer at least 1 y after PNEU-P-23. No role for booster dose.	
		Adults with HIV infection and other immunocompromising conditions	0.5 mL im once	Persons who are eligible for both conjugate and polysaccharide vaccines should receive conjugate vaccine first. However, those who have already received PNEU-P-23 may still receive PNEU-C-13, in which case administer at least 1 y after PNEU-P-23. No role for booster dose. .	
Pneumococcal vaccines, polysaccharide	*pneumococcal 23–valent polysaccharide vaccine (PNEU-P-23)*	Recommended for children ≥24 months and adults with conditions that increase risk of invasive pneumococcal disease (IPD),[b] adults ≥65 y, residents	Single 0.5 mL dose im/sc Give 8 wk after last dose of conjugate vaccine (if eligible for both). In HSCT recipients, give 6–12 months after last dose of	Persons who are eligible for both conjugate and polysaccharide vaccines should receive conjugate vaccine first.	$20

Class	Vaccine	Indications	Dose[41]	Comments	Cost[a]
	Pneumovax 23	of long-term care facilities, persons with alcoholism, smokers, homeless persons and illicit drug users	conjugate vaccine A booster dose recommended in those with asplenia, sickle cell disease, hepatic cirrhosis, chronic kidney disease or nephrotic syndrome, HIV infection, immunosuppression: ▪ after 5 y if ≥11 y of age when initially immunized ▪ after 3 y if ≤10 y of age at time of initial immunization		

a. Cost of 1 dose; includes vaccine cost only.

b. Conditions increasing risk of invasive pneumococcal disease: chronic cerebral spinal fluid leak, chronic neurologic condition that may impair clearance of secretions, cochlear implants, chronic cardiac or pulmonary disease, diabetes mellitus, chronic kidney disease, nephrotic syndrome, chronic liver disease (including hepatic cirrhosis due to any cause), asthma that required medical care in the preceding 12 months, sickle cell disease or other hemoglobinopathies, congenital immunodeficiencies, anatomic or functional asplenia, immunocompromising therapy, HIV infection, hematopoietic stem cell transplant recipient, malignant neoplasms, solid organ or islet transplant candidate or recipient.

Abbreviations: HSCT=hematopoietic stem cell transplant

Suggested Readings

Almirall J, Gonzalez CA, Balanzo X et al. Proportion of community-acquired pneumonia cases attributable to tobacco smoking. *Chest* 1999;116(2):375-9.

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.

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