Lower respiratory infections

**LOWER RESPIRATORY TRACT INFECTIONS**

Respiratory tract infections are among the most common infectious diseases. The list of causative agents continues to expand as new pathogens and syndromes are recognized. This section describes the major etiologic agents and the microbiologic approaches to the diagnosis of bronchitis and bronchiolitis; community-acquired pneumonia; healthcare-associated and ventilator-associated pneumonia; infections of the pleural space; bronchopulmonary infections in patients with cystic fibrosis; and pneumonia in the immunocompromised host. The reader is referred to various IDSA practice guidelines that have been written in recent years that describe the clinical features, diagnostic approaches, and patient management aspects of many of these syndromes.

The Key Points below summarize some important caveats when obtaining specimens for the diagnosis of respiratory infections.

**Key points** for the laboratory diagnosis of lower respiratory tract infections:

• First morning sputum is always best for culture.

• Calcium alginate swabs are not acceptable for nucleic acid amplification testing.

• Most negative rapid antigen test results should be confirmed by another method.

• Blood cultures that accompany sputum specimens may occasionally be helpful, particularly in high risk community acquired pneumonia patients.

• The laboratory should be contacted for specific instructions prior to collection of specimens for fastidious pathogens such as *Bordetella pertussis.*

• The range of pathogens causing exacerbations of lung disease in cystic fibrosis patients has expanded and specimens for mycobacterial and fungal cultures should be collected in some patients.

• In the immunocompromised host, a broad diagnostic approach based on invasively obtained specimens is suggested.

**A. Bronchitis and Bronchiolitis**

Table [VI-1](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3719886/table/CIT278TB19/) lists the etiologic agents and diagnostic approaches for acute bronchitis, acute exacerbation of chronic bronchitis and bronchiolitis, 3 clinical syndromes that involve inflammation of the tracheobronchial tree [[86](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3719886/#CIT278C86)]. Acute bronchitis is largely due to viral pathogens and is less frequently caused by *Mycoplasma pneumoniae* and *Chlamydophila pneumoniae. Bordetella pertussis* should be considered in an adolescent or young adult with prominent cough. Direct fluorescent antibody testing has been replaced by nucleic acid amplification tests (NAATs) in combination with culture as the recommended tests of choice for *B. pertussis* detection. Currently, there is one FDA cleared platform for *B. pertussis* detection. *Streptococcus pneumoniae* and *Haemophilus influenzae* do not play an established role in acute bronchitis, but they, along with *Moraxella catarrhalis,* do figure prominently in cases of acute exacerbation of chronic bronchitis. Bronchiolitis is almost exclusively caused by viruses and *M. pneumoniae.* Several FDA-approved NAAT platforms are available for the detection of select respiratory viruses.



[Table VI-1.](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3719886/table/CIT278TB19/)

Laboratory Diagnosis of Bronchitis and Bronchiolitis

**B. Community-Acquired Pneumonia**

The diagnosis of community-acquired pneumonia is based on the presence of specific symptoms and suggestive radiographic features, such as pulmonary infiltrates and/or pleural effusion. Carefully obtained microbiological data can support the diagnosis but often fails to provide an etiologic agent. Table [VI-2](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3719886/table/CIT278TB20/) lists the more common causes of community-acquired pneumonia. Other less common etiologies may need to be considered depending upon recent travel history or exposure to vectors or animals that transmit zoonotic pathogens such as Sin Nombre virus (hantavirus pulmonary syndrome) or *Yersinia pestis* (pneumonic plague, endemic in the western US).



[Table VI-2.](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3719886/table/CIT278TB20/)

Laboratory Diagnosis of Community-acquired Pneumonia

The rationale for attempting to establish an etiology is that identification of a pathogen will focus the antibiotic management for a particular patient. In addition, identification of certain pathogens such as *Legionella* species, influenza viruses, and the agents of bioterrorism have important public health significance. Currently, IDSA/ATS practice guidelines consider diagnostic testing as optional for the patient who is not hospitalized [[89](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3719886/#CIT278C89)]. Those patients who require admission should have pretreatment blood cultures, culture and Gram stain of good-quality samples of expectorated sputum and, if disease is severe, urinary antigen tests for *S. pneumoniae* and *Legionella pneumophila* where available*.* Laboratories must have a mechanism in place for screening sputum samples for acceptability (to exclude those that are heavily contaminated with oropharyngeal flora and not representative of deeply expectorated samples) prior to setting up routine bacterial culture. Poor-quality specimens provide misleading results and should be rejected because interpretation would be compromised. Endotracheal aspirates or bronchoscopically obtained samples (including “mini BAL” using the Combicath [KOL Bio Medical Instruments, Chantilly, VA] or similar technology) may be required in the hospitalized patient who is intubated or unable to produce an adequate sputum sample. A thoracentesis should be performed in the patient with a pleural effusion. Recently, the FDA approved the BioFire (Salt Lake City, UT) Film Array nucleic acid amplification test (NAAT) for detection of *Mycoplasma pneumoniae* and *Chlamydophila pneumoniae* [[90](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3719886/#CIT278C90)]. Some laboratories have developed their own NAAT assays*.* Currently, serological testing is still considered the gold standard for these agents, although this is likely to change.

Mycobacterial infections should be in the differential diagnosis of community-acquired pneumonia (CAP) that fails to respond to therapy for the typical CAP pathogens. *Mycobacterium tuberculosis,* while declining in the United States in recent years, is still an important pathogen among immigrant populations. *Mycobacterium avium* complex is also important, not just among patients with HIV, but in patients with chronic lung disease, cystic fibrosis, and in middle-aged or elderly thin women [[91](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3719886/#CIT278C91)].

**C. Healthcare-Associated Pneumonia, Hospital-Acquired Pneumonia, and Ventilator-Associated Pneumonia**

Healthcare-associated (HCAP), hospital-acquired pneumonia (HAP), and ventilator-associated (VAP) pneumonias are frequently caused by multidrug-resistant gram-negative bacteria or other bacterial pathogens. Aside from respiratory viruses that may be nosocomially transmitted, viruses and fungi are rare causes of HCAP, HA, and VAP in the immunocompetent patient. Table [VI-3](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3719886/table/CIT278TB21/) lists the organisms most commonly associated with pneumonia in the immunocompromised patient.



[Table VI-3.](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3719886/table/CIT278TB21/)

Laboratory Diagnosis of Healthcare-Associated Pneumonia, Hospital-Acquired Pneumonia and Ventilator-Associated Pneumonia

Two diagnostic strategies have been recommended by the American Thoracic Society and the Infectious Diseases Society of America [[92](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3719886/#CIT278C92)]. The clinical strategy is based on the presence of a new lung infiltrate plus the presence of 2 of 3 clinical features (fever, leukocytosis or leucopenia, and purulent secretions) [[92](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3719886/#CIT278C92)]. Determining the cause of the pneumonia relies on initial Gram stain and semiquantitative cultures of endotracheal aspirates or sputum. A smear lacking inflammatory cells and a culture absent of potential pathogens have a very high negative predictive value. Cultures of endotracheal aspirates, while likely to contain the true pathogen, also consistently grow more mixtures of species of bacteria than specimens obtained by bronchoscopic techniques. This may lead to additional unnecessary antibiotic therapy. The bacteriologic strategy uses quantitative cultures of lower respiratory tract secretions obtained either bronchoscopically or via endotracheal aspiration without a bronchoscope [[92](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3719886/#CIT278C92)]. Quantities of bacterial growth above a threshold are diagnostic of pneumonia and quantities below that threshold are more consistent with colonization. The generally accepted thresholds are as follows: Endotracheal aspirates, 106 CFU/mL; BAL, 104 CFU/mL; protected specimen brush samples (PSB), 103 CFU/mL. These values have significance only when the samples have been obtained >72 hours before the initiation or a change of antibiotic therapy. Quantitative studies require extensive laboratory work and special procedures that smaller laboratories may not accommodate. Bronchial washes are not appropriate for routine bacterial culture

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**Table VI-3.**

Laboratory Diagnosis of Healthcare-Associated Pneumonia, Hospital-Acquired Pneumonia and Ventilator-Associated Pneumonia

| **Etiologic Agents** | **Diagnostic Procedures** | **Optimum Specimens** | **Transport Issues; Optimal Transport Time** |
| --- | --- | --- | --- |
| **Bacteria** |
| *Pseudomonas aeruginosa* | Blood culture | Blood cultures | Sterile cup or tube RT, 2 h; 4°C, >2–24 h |
| *Escherichia coli* | Gram stain | Sputum |
| *Klebsiella pneumoniae* | Quantitative or semi-quantitative aerobic and anaerobic culturea | Endotracheal aspirates |
| *Enterobacter* spp | BAL |
| *Serratia marcescens* | Protected specimen brush samplesa |
| *Acinetobacter* spp | Lung tissue |
| *Stenotrophomonas maltophilia* |
| *Staphylococcus aureus* and MRSA |
| *Haemophilus influenzae* |
| *Streptococcus pneumoniae* | As above plus urine antigenb | Urine | Sterile container RT, 24 h; >24 h–14 d, 2–8°C |
| Mixed anaerobes (aspiration) | Gram stain | Protected specimen brush samplesa | Sterile tube with 1 mL of thioglycolate (for brush samples); Sterile container for tissue; RT, 2 h; 4°C, >2–24 h |
| Culturea | Lung tissue |
| *Legionella* spp | Culture on BCYE media | Induced sputum | Sterile cup or tube RT, 2 h; 4°C, >2–24 h |
| NAATc | Endotracheal aspirates |
| BAL |
| Protected specimen brush samples |
| Lung tissue |
| Urine antigen (*L. pneumophila* serogroup 1 only) | Urine | Sterile container RT, <24 h; 4°C >24 h–14 d |
| **Fungi** |
| *Aspergillus* spp | Fungal stain—KOH with calcofluor; other fungal stains | Endotracheal aspirates | Sterile cup or tube RT, 2 h; 4°C, >2–24 h |
| Fungal culture | BAL |
| Protected specimen brush samples |
| Histology | Lung tissue | Sterile cup; RT, 2 h; or formalin container, RT, 2–14 d |
| Galactomannand (1–3) β-D-glucans | Serum, | Clot tube 4°C, ≤5 d; >5 d, −70°C |
| BALe | Sterile cup or tube RT, 2 h; 4°C, >2–24 h |
| **Viruses** |
| Influenza viruses A, B | Rapid antigen detection | Nasal washes, aspirates | Transport in viral transport media, RT or 4°C, 5 d; −70°C, >5 d |
| Parainfluenza viruses | Viral culture methods | NP swabs |
| Adenovirus | NAATf | Endotracheal aspirates |
| Respiratory syncytial virus | Bronchoalveolar lavage |
| DFA | Protected specimen brush samples |

[View it in a separate window](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3719886/table/CIT278TB21/?report=objectonly)

Abbreviations: BAL, bronchoalveolar lavage; BCYE, buffered charcoal yeast extract; DFA, direct fluorescent antibody; KOH, potassium hydroxide; MRSA, methicillin-resistant *Staphylococcus aureus*; NAAT, nucleic acid amplification test; NP, nasopharyngeal; RT, room temperature.

a Anaerobic culture should only be done if the specimen has been obtained with a protected brush or catheter and transported in an anaerobic transport container or by placing the brush in 1 mL of pre-reduced broth prior to transport.

b Sensitivity in nonbacteremic patients with pneumococcal pneumonia is 52%–78%; sensitivity in bacteremic cases of pneumococcal pneumonia is 80%–86%; specificity in adults is >90%. However, studies have reported a 21%–54% false positive rate in children with NP carriage and no evidence of pneumonia [[87](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3719886/#CIT278C87)].

c No FDA cleared test is currently available. Availability is laboratory specific. Provider needs to check with the laboratory for optimal specimen source, performance characteristics and turnaround time.

d Performance characteristics of these tests are reviewed in reference [[93](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3719886/#CIT278C93)].

e Testing from this source is not offered in all microbiology laboratories.

f Several FDA cleared NAAT platforms are currently available and vary in their approved specimen requirements and range of analytes detected. Readers should check with their laboratories regarding availability and performance characteristics including certain limitations.

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