INTRODUCTION AND EPIDEMIOLOGY

Bacterial and viral infections of the respiratory tract can result in a wide range of clinical syndromes including acute bronchitis, the common cold, influenza, and respiratory distress syndromes. Uniform definitions for the most common of these clinical syndromes are lacking because the symptoms associated with upper respiratory tract infections (URIs) frequently overlap and their causative pathogens are similar. The broad definition of acute bronchitis is as follows: a self-limited inflammation of the large airways characterized by cough without evidence of pneumonia, without an alternative medical disorder to explain the symptoms, or without a history of chronic lung disease.¹

The common cold is a viral infection of the upper respiratory tract, primarily affecting the nasal mucosa, causing congestion, rhinorrhea, and sneezing. Influenza, or the "flu," is a respiratory illness caused by influenza viruses. Symptoms of influenza infection range from mild to severe and include fever, chills, myalgias, headache, malaise, cough, and fatigue. Severe acute respiratory syndrome is a unique respiratory illness that has clinical characteristics similar to other URIs but confers a high rate of mortality. Reported in 2012, Middle East respiratory syndrome coronavirus is novel viral respiratory infection that became a concern to the World Health Organization due to its fatality rate. Infections of the upper respiratory tract also cause specific clinical conditions like otitis media, pharyngitis, epiglottitis, bronchiolitis, laryngitis, tracheitis, and sinusitis (see corresponding chapters that discuss these diseases).

EPIDEMIOLOGY

In ambulatory care settings nationwide, URIs are the third most common diagnosis.² Annually, the estimated direct costs of noninfluenza viral URI in the United States is $17 billion, with indirect costs exceeding $22 billion.³ Acute bronchitis is among the most commonly diagnosed outpatient illnesses in the United States every year, with an annual incidence of about 5%,⁴ predominantly during fall and winter.¹ The disorder accounts for approximately 10 million office visits per year, or 10 ambulatory visits per 1000 people per year. Symptom relief is the primary reason for office visits among adults within the first 2 weeks of illness, and many of these visits result in the unnecessary prescription of antibiotics by clinicians.⁵ The common cold afflicts adults two or three times every year, whereas children suffer up to eight colds annually.⁶,⁷,⁸ The
incidence of colds caused by rhinovirus peaks during autumn months. Responsible for 22 million missed school days and 23 million lost work days, the common cold generates an enormous economic burden.

Influenza affects millions of people worldwide every year during seasonal outbreaks (typically November through March in the northern hemisphere). An annual average of 41,000 Americans died from influenza infection from 1979 to 2001. The Centers for Disease Control and Prevention reported influenza-associated annual death rates between 1976 and 2007 that ranged from 1.4 to 16.7 deaths per 100,000 persons. Deaths associated with influenza have increased in recent decades in the United States. With 90% of influenza-associated deaths occurring among people 65 years or older, influenza poses a particular threat to the elderly. In 2009, an outbreak of swine-origin influenza A (H1N1) virus, known as "swine flu," occurred in Mexico and the United States.

Influenza viruses are classified into three genera: A, B, and C. Of these, influenza A has the greatest impact on human populations and has the greatest potential to cause pandemics. Influenza A has many serotypes, including H1N1 and H3N2, both of which are currently active among humans. Influenza viruses are unique pathogens because their evolution involves a complex process of antigenic shifts and sporadic cross-species transmissions between humans, swine, and birds. The intensity of seasonal influenza varies from one year to the next, and localized influenza outbreaks can occur during interpandemic years. Furthermore, seasonal influenza outbreaks tend to occur simultaneously in countries on similar latitudes. Population immunity against influenza can be achieved by natural infection or vaccination; however, antigenic shifts allow influenza viruses to survive from year to year and preserve their capacity to cause global pandemics.

**ACUTE BRONCHITIS**

**PATHOPHYSIOLOGY**

Etiologic studies of acute bronchitis are difficult to interpret because the disease lacks a precise definition and the cause is undetermined in 31% to 84% of cases vigorously tested. Respiratory viruses are the most common causative agents, with confirmed cases in 9% to 63% of patients studied, depending on the criteria used to make the diagnosis and the population. Influenza A and B viruses are the most common cause, accounting for 6% to 35% of cases. Parainfluenza virus, respiratory syncytial virus, coronavirus, adenovirus, rhinovirus, and human metapneumovirus combined account for another third of cases. Bacterial causes of acute bronchitis range from less than 10% to as much as 44% of cases in studies of older populations with comorbidities and severe symptoms. *Streptococcus pneumoniae* (0% to 30% of cases), *Haemophilus influenzae* (0% to 9% of cases), and *Moraxella catarrhalis* (0% to 2% of cases) have been isolated in patients with acute bronchitis. Atypical bacterial species such as *Bordetella pertussis* (0% to 1%), *Chlamydia pneumoniae* (0% to 17%), and *Mycoplasma pneumoniae* (1% to 10%) also cause acute bronchitis.
There are two overlapping sequential phases in the pathophysiology of acute bronchitis. The first phase results from the direct inoculation of the tracheobronchial epithelium, yielding variable constitutional symptoms of fever, myalgias, malaise, and organism-specific upper respiratory symptoms, lasting 1 to 5 days, the severity of which depends on the infectious agent. The second phase is characterized by hypersensitivity of the tracheobronchial epithelium and airway receptors resulting in persistent, productive cough and lasting 1 to 3 weeks, peaking at 7 to 14 days. It is this second phase that best characterizes the illness. Sloughed epithelial cells and increased mucus produce sputum in most patients; sputum is not an indication of ongoing bacterial infection as frequently suspected by clinicians. Inflammation and thickening of the bronchial and tracheal mucosa (Figure 64–1) result in airflow obstruction and decreased forced expiratory volume in 1 second, manifesting as wheezing and dyspnea in many patients.

**FIGURE 64–1.**
The respiratory epithelial infection of acute bronchitis leads to inflammation, thickening, and increased mucus production in the airways.

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CLINICAL FEATURES
The clinical manifestations of acute bronchitis depend on the infectious agent, especially in the first phase of the illness. Therefore, the initial symptoms are variable and may include fever, dyspnea, myalgias, malaise, sore throat, nasal congestion, and cough. The hallmark of acute bronchitis is cough (with or without phlegm production) persisting into the second phase of the illness lasing more than 5 days and up to 3 or 4 weeks. The mean duration of cough is 18 days. During this phase, the patient may or may not have dyspnea and/or chest discomfort. Physical exam may be completely normal, or the patient may have tachypnea, tachycardia, fever, wheezing, rhonchi, or rales. One important etiology of acute bronchitis to identify is *Bordetella pertussis*, because antibiotic treatment is recommended (see later discussion).

Suspect pertussis in patients with posttussive emesis or inspiratory whoop; consider pertussis in any patient with cough lasting greater than 2 weeks if exposed to a known case or presenting during an epidemic.

**DIAGNOSIS**

The diagnosis of acute bronchitis is made using clinical findings and historical information: when acute cough (dry or productive) is present for more than 5 days and when evidence of pneumonia, acute asthma, or an alternative explanation for the symptoms is absent. Patients with chronic obstructive pulmonary disease are excluded from the diagnosis (see chapter 70, Chronic Obstructive Pulmonary Disease).

The primary objective in patient evaluation is carefully excluding pneumonia, either clinically or radiographically. Physicians are poor at differentiating patients with pneumonia from patients with bronchitis based on history and physical exam. The addition of C-reactive protein testing does not improve diagnostic accuracy. Identification of patients at low risk for pneumonia may be accomplished based on the absence of vital sign abnormalities and physical exam findings. See Table 64–1 for criteria suggesting pneumonia; patients meeting none of these criteria have a probability of pneumonia of 5% or less, and further testing is not required provided the patient has follow-up in the next 3 days and is able to return to the ED if symptoms worsen. Patients with hypoxia or unstable vital signs (in the setting of respiratory symptoms) are at high risk for pneumonia and require further testing and treatment (see chapter 65, Pneumonia and Pulmonary Infiltrates). Obtain a chest radiograph in patients at intermediate risk for pneumonia. Although chest radiography remains the most common confirmatory test for pneumonia, the sensitivity of a standard two-view chest film ranges from 69% in symptomatic patients suspected of pneumonia in the community, to as low as 43.5% in patients being evaluated for pulmonary embolism in the ED (both studies using high-resolution CT scan as the criterion reference). Therefore, if pneumonia is suspected on clinical grounds, treat accordingly regardless of a negative chest radiograph (see chapter 65) especially in the elderly, among whom distinctive signs and symptoms of pneumonia may be lacking. Laboratory tests should be obtained if treatment for *B. pertussis* is being planned; tests include a culture, using a Dacron swab specimen, collected from the posterior nasopharynx; performing direct fluorescent antibody staining; collecting a polymerase chain reaction test; or testing for serum antibodies by enzyme-linked immunosorbent assays or Western blot. Otherwise, further testing for acute bronchitis is
not necessary unless alternative diagnoses require investigation. The differential diagnosis of cough is broad; see Table 64-5, Differential of Consequence: Cough, in chapter 62, Respiratory Distress.

Table 64–1

Clinical Criteria Suggesting Possible Pneumonia

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Clinical Finding</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Heart rate &gt;100 beats/min</td>
</tr>
<tr>
<td>2</td>
<td>Respiratory rate &gt;24 breaths/min</td>
</tr>
<tr>
<td>3</td>
<td>Temperature of &gt;38°C (100.4°F)</td>
</tr>
<tr>
<td>4</td>
<td>Chest examination findings of focal consolidation, egophony (increased resonance of voice sounds heard when auscultating the lungs), or fremitus (tactile vibrations felt over the chest when the patient repeats &quot;boy oh boy&quot;)</td>
</tr>
<tr>
<td>5</td>
<td>Age &gt; 64 y old</td>
</tr>
</tbody>
</table>

All five criteria must be absent in an individual patient to lower the probability of pneumonia to 5% or less.

TREATMENT

Case definitions of acute bronchitis that specify constitutional or respiratory symptoms including characteristics of sputum are used by research investigators and can define the spectrum of microbiologic causes but have not identified a patient subset that clearly benefits from antibiotics (see Acute Bronchitis, Treatment, later in this chapter).

Despite the fact that some patients with acute bronchitis have evidence of a bacterial infection in epidemiologic studies, antibiotics are not beneficial and are not indicated except in isolated cases. A Cochrane analysis reviewed 15 randomized controlled trials, involving 2618 patients, including smokers and nonsmokers, comparing any antibiotic versus placebo or no treatment for acute bronchitis. At follow-up, patients receiving antibiotics were less likely to have cough (relative risk 0.64; 95% confidence interval 0.49 to 0.85), were less likely to have abnormal lung exam findings (relative risk 0.54; 95% confidence interval 0.41 to 0.70), experienced fewer days of feeling ill (mean difference –0.64; 95% confidence interval –1.16 to –0.13), and had fewer days with limited activity (mean difference –0.49; 95% CI –0.94 to –0.04). Although the differences between these outcome measures reached statistical significance, the benefits demonstrated were modest (less than 1-day benefit in an illness lasting 10 to 21 days). Consider potential medication side effects, cost, and the potential for microbial resistance when using antibiotics to achieve these modest
benefits for an otherwise self-limiting illness. Despite the lack of evidence supporting their use, the majority of acute bronchitis patients receive antibiotics, especially elderly patients and smokers.\textsuperscript{1,5,38,40,41,42}

To counter public perception and patients' prior experiences with antibiotics, offer patient education.\textsuperscript{43} Both printed and computer-assisted patient educational intervention reduce antibiotic prescriptions in the primary care setting.\textsuperscript{44} For confirmed or presumed \textit{B. pertussis} infection give azithromycin (500 milligrams on day 1, 250 milligrams on days 2 to 5) to prevent transmission to contacts.\textsuperscript{1,5,27} For influenza, if the patient presents very early in the course and influenza is suspected as the cause, consider influenza-specific antiviral therapy (see later section, \textit{Influenza}).

There is little evidence to support the routine use of $\beta_2$-agonists for acute bronchitis in the absence of wheezing on physical exam.\textsuperscript{1,5,39} A Cochrane Review reported no significant differences in daily cough scores or in duration of cough among adults with acute bronchitis who received $\beta_2$-agonists versus placebo or no treatment. Adults treated with $\beta_2$-agonists were more likely to report adverse effects such as tremor, shakiness, and nervousness (relative risk 7.94; 95\% confidence interval 1.17 to 53.94).\textsuperscript{45} However, among patients with evidence of airflow obstruction, $\beta_2$-agonists result in lower symptom scores and faster cough resolution.\textsuperscript{45} Therefore, consider bronchodilators in acute bronchitis patients with wheezing.\textsuperscript{46} Antihistamines do not reduce mean cough scores in acute bronchitis. Limited data are available on the efficacy of antitussives for acute bronchitis, and no data exist on the value of oral corticosteroids in nonasthmatics with acute bronchitis.\textsuperscript{47} Dextromethorphan and codeine preparations may be no more effective than placebo in improving symptoms or reducing cough severity in acute bronchitis.\textsuperscript{38} If used, limit antitussive therapy to those patients with a cough causing discomfort where inhibition of airway secretion clearance will not compromise breathing.\textsuperscript{46}

**COMMON COLD**

**PATHOPHYSIOLOGY**

The pathogens responsible for causing the common cold include rhinovirus, adenovirus, parainfluenza virus, respiratory syncytial virus, enterovirus, and coronavirus. The rhinovirus, a species of the \textit{Enterovirus} genus of the \textit{Picornaviridae} family, is the most common cause of the common cold and causes up to 80\% of all respiratory infections during peak seasons.\textsuperscript{8,9,48} Dozens of rhinovirus serotypes and frequent antigenic changes among them make identification, characterization, and eradication exceedingly complex. After deposition in the anterior nasal mucosa, rhinovirus replication and infection are thought to begin upon mucociliary transport to the posterior nasopharynx and adenoids. As soon as 10 to 12 hours after inoculation, symptoms may begin. The mean duration of symptoms is 7 to 10 days, but symptoms can persist for as long as 3 weeks.\textsuperscript{9} Nasal mucosal infection and the host's subsequent inflammatory response cause
vasodilation and increased vascular permeability. These events result in nasal obstruction and rhinorrhea, whereas cholinergic stimulation prompts mucus production and sneezing.

CLINICAL FEATURES

Patients afflicted with the common cold can experience nasal congestion, rhinorrhea, sneezing, sore throat, cough, and malaise. Clinical signs of rhinovirus infection include nasal discharge and hoarse voice. The consistency and purulence of nasal discharge in patients with the common cold do not necessarily indicate a bacterial infection. The high incidence of sinus abnormalities in patients with uncomplicated colds makes the identification of true bacterial sinusitis challenging. Sinusitis is estimated to complicate rhinovirus illness in 0.5% to 2% of cases (see chapter 244, Nose and Sinuses). Although fever is a common finding in children with rhinovirus infection, fever is uncommon in adults. Middle ear effusions may be noted, particularly among children, in whom acute otitis media occurs in up to 20% of viral URIs.

DIAGNOSIS

The presence of classical features for rhinovirus infection, coupled with the absence of signs of bacterial infection or serious respiratory illness, is sufficient to make the diagnosis of the common cold. The common cold is a clinical diagnosis, and diagnostic testing is not necessary.

TREATMENT

The goal of treatment for the common cold is symptom relief. Decongestants and combination antihistamine/decongestant preparations can decrease cough, congestion, and other symptoms in adults. Avoid cough preparations in children. H1-receptor antagonists may offer a modest reduction of rhinorrhea and sneezing during the first 2 days of a cold in adults. First-generation antihistamines are sedating, so advise the patient about caution during their use. Topical and oral nasal decongestants (i.e., topical oxymetazoline, oral pseudoephedrine) have moderate benefit in adults and adolescents in reducing nasal airway resistance. Evidence-based data do not support the use of antibiotics in the treatment of the common cold because they do not improve symptoms or shorten the course of illness. There is also a lack of compelling evidence supporting the use of dextromethorphan for acute cough.

According to a Cochrane Review, vitamin C used as daily prophylaxis at doses of ≥0.2 grams or more had a "modest but consistent effect" on the duration and severity of common cold symptoms (8% and 13% decreases in duration for adults and children, respectively). When taken therapeutically after the onset of symptoms, however, high-dose vitamin C has not shown clear benefit in trials. Echinacea is an herbal remedy commonly used for treating the common cold; at this time, there is no clear evidence that echinacea is effective. Zinc has also been proposed for the treatment of common cold symptoms, and a meta-analysis found that oral zinc lozenges may shorten the course of symptoms in adults (no benefit in children), but
nausea and altered taste were common, and the authors cautioned against a generalized recommendation.\textsuperscript{54}

**INFLUENZA**

**PATHOPHYSIOLOGY**

The incubation period for influenza is 1 to 4 days, and the time interval between symptom onset among related household cases is estimated to be 3 to 4 days. Viral shedding can occur 1 day before the onset of symptoms. Shedding generally decreases by 3 to 5 days after illness in adults but can continue for more than 10 days after illness onset in children.\textsuperscript{55} Understanding the routes of influenza transmission is critical to the development of effective infection control guidelines and for the planning of global, regional, and local pandemic responses. A debate exists over the route(s) of influenza virus transmission in mammals. It is believed that influenza can be transferred among humans by direct contact, indirect contact, droplets, or aerosolization. Short distances (<1 m) are generally required for contact and droplet transmission to occur between the source person and the susceptible individual. Airborne transmission may occur over longer distances (>1 m). Experimental and observational studies support the possibility of influenza transmission by all of these routes. However, most evidence-based data suggest that direct contact and droplet transfer are the predominant modes of transmission for influenza.\textsuperscript{56}

**CLINICAL FEATURES**

Influenza infection is characterized by abrupt onset of fever, headache, dry cough, sore throat, myalgias, and rhinitis. Oropharyngeal irritation and mild cervical lymphadenopathy may be present. Although the presence of fever can help distinguish influenza from the common cold, up to one third of H1N1 influenza cases in 2009 demonstrated flu symptoms without fever.\textsuperscript{55} Hence, influenza can be difficult to distinguish from other viral URIs. Fever and intense myalgias are generally more prevalent in influenza infection than other viral URIs. Healthy individuals with uncomplicated influenza illness will generally experience resolution of symptoms in 3 to 7 days, although cough and malaise may persist beyond 2 weeks (see earlier section, *Acute Bronchitis*).

**DIAGNOSIS**

During seasonal influenza outbreaks, most cases of influenza can be diagnosed on clinical grounds alone. A retrospective analysis of 3744 subjects showed that the development of cough and fever are the best multivariate predictors of influenza infection with a positive predictive value of 79% \((P<0.001)\).\textsuperscript{57} During interpandemic periods, clinical signs and symptoms may be less predictive of sporadic influenza infection, and management decisions may be aided by diagnostic testing.

If the diagnostic test result for influenza will influence management decisions, certain patients should undergo testing. When signs of influenza infection are present *during an influenza outbreak*, perform testing on hospitalized patients, patients with high-risk conditions, and patients for whom a positive result would
impact clinical care decisions. When a patient presents with signs of influenza infection at any time of year, consider testing for (1) healthcare personnel or visitors linked to an influenza outbreak presenting within 5 days of illness and (2) patients who are epidemiologically linked to an influenza outbreak presenting within 5 days of symptom onset.\textsuperscript{58}

When testing for influenza, obtain specimens as close to symptom onset as possible. Nasal aspirates and swabs are the best specimens to obtain when testing infants and young children. For older children and adults, swabs and aspirates from the nasopharynx are preferred. Additional specimens from endotracheal aspirates and/or bronchoalveolar lavage fluid should be obtained from ventilated patients to allow testing of the lower respiratory tract.\textsuperscript{58} Several influenza tests are available for clinical use (Table 64–2). Given their ability to provide results rapidly (<30 minutes), commercially available rapid influenza diagnostic tests are most practical in the ED. However, with reported sensitivities of these kits ranging from 10% to 80% (specificity 85% to 100%), negative rapid influenza tests do not completely exclude infection.\textsuperscript{58,59}
### Influenza Testing Modalities

<table>
<thead>
<tr>
<th>Test</th>
<th>Time to Results</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapid influenza test–antigen detection (EIA)</td>
<td>10–20 min</td>
<td>70%–90% sensitivity in children, &lt;40%–60% sensitivity in adults, follow-up testing with RT-PCR should be considered to confirm negative result</td>
</tr>
<tr>
<td>Rapid influenza test–neuraminidase detection assay</td>
<td>20–30 min</td>
<td>Detects but does not distinguish between influenza A and B</td>
</tr>
<tr>
<td>RT-PCR</td>
<td>2 h</td>
<td>High sensitivity and specificity, highly recommended test for influenza</td>
</tr>
<tr>
<td>Immunofluorescence</td>
<td>2–4 h</td>
<td>Direct and indirect immunofluorescent antibody staining detects and distinguishes between influenza A/B and other viruses</td>
</tr>
<tr>
<td>Viral culture–shell vial</td>
<td>48–72 h</td>
<td>Viral isolation/cultures are not screening tests; highest specificity, moderately high sensitivity; useful for confirming screening tests and surveillance purposes</td>
</tr>
<tr>
<td>Viral culture–cell culture isolation</td>
<td>3–10 d</td>
<td></td>
</tr>
</tbody>
</table>

**Abbreviations:** EIA, enzyme immunoassay; RT-PCR, reverse transcription polymerase chain reaction.


### TREATMENT

Early antiviral treatment for influenza infection shortens the duration of influenza symptoms, decreases the length of hospital stays, and reduces the risk of complications. Recommendations for the treatment of influenza are updated frequently by the Centers for Disease Control and Prevention based on epidemiologic data and antiviral resistance patterns. The treatment of influenza infection is recommended as early as possible for any patient with confirmed or suspected influenza who (1) is at high risk for influenza complications (*Table 64–3*), (2) has severe, complicated or progressive illness, or (3) is hospitalized.
Table 64–3

Persons at Higher Risk for Complications of Influenza Infection

- Children <5 y (especially <2 y)
- Adults ≥65 y
- Persons with chronic illnesses and/or conditions*
- Persons with immunosuppression, including secondary to human immunodeficiency virus infection or medications
- Women who are pregnant or postpartum (within 2 weeks of delivery)
- Persons <18 y receiving long-term aspirin therapy
- Residents of nursing homes and other chronic care facilities
- Persons who are morbidly obese (body mass index ≥40)
- American Indians/Alaska Natives

*Includes persons with chronic pulmonary (including asthma, cystic fibrosis), cardiovascular (except hypertension alone), renal, hematologic (including sickle cell disease), and hepatic diseases; metabolic disorders (including diabetes mellitus); cancers; or neurologic and neurodevelopment conditions including disorders of the brain, spinal cord, peripheral nerve, and muscle such as cerebral palsy, epilepsy (seizure disorders), stroke, intellectual disability (mental retardation), moderate to severe developmental delay, muscular dystrophy, or spinal cord injury.

A patient who does not meet the above criteria may still require treatment depending on clinical circumstances and clinician concern. Give antiviral therapy for influenza within 48 hours of symptom onset (or earlier), and do not delay treatment for laboratory confirmation if a rapid test is not available. Antiviral treatment can provide benefit even after 48 hours in pregnant and other high-risk patients.\(^{61,62}\) Therefore, consider antiviral treatment even 3 or 4 days after onset of illness in certain high-risk populations.\(^{60}\)

For the 2012 to 2013 influenza season, the neuraminidase inhibitors zanamivir and oseltamivir were recommended by the Centers for Disease Control and Prevention for the prevention and treatment of influenza infection\(^{55,60}\) (see Table 64–4 for dosing recommendations). The recent development of resistance among several influenza strains to the neuraminidase inhibitors emphasizes the importance of following updated epidemiologic reports and recommendations by the Centers for Disease Control and Prevention and other health agencies.
Table 64–4

**Neuraminidase Inhibitor Dosing Recommendations**

<table>
<thead>
<tr>
<th><em><em>Oseltamivir (Tamiflu</em>)</em>*</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Treatment</strong></td>
<td><strong>Chemoprophylaxis</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Adults</strong></td>
<td>75 milligrams twice daily × 5 d*</td>
<td>75 milligrams once daily × 7 d†</td>
</tr>
<tr>
<td><strong>Children‡</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;15 kg</td>
<td>30 milligrams twice daily × 5 d*</td>
<td>30 milligrams once daily × 7 d</td>
</tr>
<tr>
<td>15–23 kg</td>
<td>45 milligrams twice daily × 5 d*</td>
<td>45 milligrams once daily × 7 d</td>
</tr>
<tr>
<td>24–40 kg</td>
<td>60 milligrams twice daily × 5 d*</td>
<td>60 milligrams once daily × 7 d</td>
</tr>
<tr>
<td>&gt;40 kg</td>
<td>75 milligrams twice daily × 5 d*</td>
<td>75 milligrams once daily × 7 d</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><em><em>Zanamivir (Relenza</em>)</em>*</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Treatment</strong></td>
<td><strong>Chemoprophylaxis</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Adults</strong></td>
<td>10 milligrams (2 inhalations) twice daily × 5 d*</td>
<td>10 milligrams (2 inhalations) once daily × 7 d†</td>
</tr>
<tr>
<td><strong>Children‡</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥5 y old#</td>
<td>N/A</td>
<td>10 milligrams (2 inhalations) once daily</td>
</tr>
<tr>
<td>≥7 y old</td>
<td>10 milligrams (2 inhalations) twice daily × 5 d*</td>
<td>10 milligrams (2 inhalations) once daily × 7 d†</td>
</tr>
</tbody>
</table>

* Longer courses can be considered for patients who remain severely ill after 5 days of treatment.

† For controlling outbreaks in long-term care facilities, the Centers for Disease Control and Prevention recommend a minimum of 2 weeks of chemoprophylaxis and up to 1 week after the last identified case, and 7 days after most recent known exposure in other cases.
Antiviral medications are not Food and Drug Administration approved for treatment or prophylaxis of influenza in children age <12 months. Limited data are available in this age group. Oseltamivir was used in infants during the 2009 influenza A (H1N1) pandemic under Emergency Use Authorization (expired June 2010).

Zanamivir is approved for treatment of influenza in children age $\geq$7 years and for influenza chemoprophylaxis in children age $\geq$5 years.

Vaccination is the most effective method of preventing influenza illness. Antiviral chemoprophylaxis is also helpful in preventing influenza (70% to 90% effective) and should be considered as an adjunct to vaccination in certain scenarios or when vaccination is unavailable or not possible. Generally, antiviral chemoprophylaxis is used during periods of influenza activity for (1) high-risk persons who cannot receive vaccination (due to contraindications) or in whom recent vaccination does not, or is not expected to, afford a sufficient immune response; (2) controlling outbreaks among high-risk persons in institutional settings; and (3) high-risk persons with influenza exposures.$^{58,60}$ For more information about the indications for antiviral chemoprophylaxis, consult the Centers for Disease Control and Prevention website (http://www.cdc.gov/flu). Widespread and routine use of chemoprophylaxis is discouraged due to the possibility of promoting resistance and depleting supplies for high-risk or critically ill patients during influenza outbreaks.

**DISEASE COMPLICATIONS**

Complications of influenza infection include primary influenza viral pneumonia; secondary bacterial pneumonia; sinusitis; otitis media; coinfection with bacterial agents; and exacerbation of preexisting medical conditions, particularly asthma and chronic obstructive pulmonary disease. Pneumonia is one of the most common complications of influenza illness in children and contributes significantly to morbidity and mortality. Children who develop pneumonia in association with influenza are more likely to develop respiratory failure (11% vs. 3%), require intensive care unit admission (21% vs. 11%), and die (0.9% vs. 0.3%).$^{63}$

**SEVERE ACUTE RESPIRATORY SYNDROME (SARS)**

Severe acute respiratory syndrome is a rapidly progressive illness caused by a coronavirus, the severe acute respiratory syndrome coronavirus. Emerging in China in November 2002, severe acute respiratory syndrome quickly became a global health concern by early 2003. The World Health Organization reported 8096 probable severe acute respiratory syndrome cases worldwide through April 21, 2004. Deaths attributed to severe acute respiratory syndrome totaled 774 during that time period (9.6% case fatality rate).$^{64}$ Isolation procedures for suspected severe acute respiratory syndrome patients include airborne, droplet, and contact isolation. Healthcare providers should wear an N95 or higher respiratory facemask when caring for patients with severe acute respiratory syndrome, in addition to glove, gown, and eye protection.

Although severe acute respiratory syndrome shares many clinical features with viral URIs, its clinical characteristics are ill-defined, and case definitions were updated frequently during its emergence. The
Clinical features of coronavirus infection include fever (99% frequency), nonproductive cough, dyspnea, myalgias, headache, and diarrhea. Many cases progress to a moderate-severe condition characterized by hypoxia and dyspnea at rest. Respiratory failure requiring mechanical ventilation occurs in 10% to 20% of hospitalized patients with severe acute respiratory syndrome. Risk factors for death in coronavirus infection include age >60 years, diabetes mellitus, and hepatitis B infection.65

Consider the diagnosis of severe acute respiratory syndrome on clinical grounds when the patient has been exposed to known cases or has traveled to regions with severe acute respiratory syndrome activity. Chest radiographs may show subtle peripheral pulmonary infiltrates. Chest CT demonstrates ground-glass consolidation during early phases of illness. Lymphopenia, thrombocytopenia, elevated lactic dehydrogenase, liver enzymes, and creatine phosphokinase levels have been reported but are not pathognomonic for severe acute respiratory syndrome.66 When severe acute respiratory syndrome is suspected, collect two specimens (from different locations) for polymerase chain reaction testing and obtain serum for serologic testing. To date, several diagnostic tests are available to detect coronavirus, but each has substantial limitations in sensitivity, specificity, or clinical practicality. Treatment for severe acute respiratory syndrome is largely supportive. When lopinavir-ritonavir was added to standard therapy (ribavirin and corticosteroids) for severe acute respiratory syndrome during a nonrandomized, open-label study in Hong Kong, a significant reduction in death rate was noted. Limitations in this study, however, make it difficult to derive definitive conclusions about its efficacy.65

**MIDDLE EAST RESPIRATORY SYNDROME CORONAVIRUS (MERS)**

In the summer of 2012, in Jeddah, Saudi Arabia, a novel coronavirus was isolated from the sputum of a patient with pneumonia and renal failure.67 Since that time, the virus has been named the Middle East respiratory syndrome coronavirus. As of August 30, 2013, there have been 108 reported cases (several still hospitalized at that time) and 50 deaths.68 All cases have been directly or indirectly linked to one of four countries: Saudi Arabia, Qatar, Jordan, and the United Arab Emirates, with the largest number from Saudi Arabia.69 The original source is suspected to have come from bats.70 Median age of patients is 56 years (range 2 to 94 years). All patients had respiratory symptoms, and some had GI symptoms including abdominal pain and diarrhea. The majority of patients experience severe acute respiratory disease requiring hospitalization; the case fatality rate has been reported as 56%. In addition to respiratory failure, renal failure and septic shock are common causes of death. Several patients had significant preexisting comorbidities, including immunosuppression. Cases have included healthcare workers and family contacts. A documented patient-to-patient nosocomial transmission has been reported in France.71 Treatment is supportive and frequently requires mechanical ventilation, dialysis, and extracorporeal membrane oxygenation. Nonspecific antiviral drugs have been used, such as ribavirin, lopinavir, and type I interferon, but their efficiency is still unclear.72 Patients should be isolated in an airborne infection isolation room.73 Healthcare workers should wear personal protective equipment including gloves, gown, eye protection, and a fit-tested N95 respirator facemask.73
PERTUSSIS

Pertussis, or "whooping cough," is an acute respiratory infection in humans caused by the aerobic gram-negative rod, *B. pertussis*. Pertussis toxins cause respiratory epithelial and mucosal injury and interfere with immune cell function. Pertussis pneumonia can occur in children, but in school-age children, adolescents, and adults, URIs are the rule.

IMMUNIZATION

Although pertussis is often considered a disease of infants (primarily in those <1 year old who have not completed three doses of vaccination) and a disease in developing countries where immunization is not universal, in North America, the disease is now more common in school-age children and adults. School-age children are the usual sources of infection, and adults may serve as carriers of disease. Cyclical outbreaks occur every 3 to 5 years despite widespread immunization practices.

There are two types of vaccines, whole-cell and acellular. Whole-cell pertussis vaccination is effective for about 10 years and is used in developing nations. The acellular diphtheria, tetanus, and pertussis vaccine (DTaP), developed to remove toxins from the cell membrane, does not protect as long as the whole-cell vaccine and is typically used in the developed world. The typical immunization schedule is at 2, 4, 6, and 18 months of age and a booster at age 5. Adolescents should receive a DTaP booster. Pregnant women should receive a booster of DTaP to protect neonates and infants and to prevent infection in the mother. For the unimmunized elderly (>65 years old), one dose of DTaP is recommended. Although the vaccine is specifically not registered for the elderly, a study of nearly 120,000 individuals ≥65 years old did not demonstrate any increase in inflammatory or allergic events in those receiving DTaP compared with those receiving only the tetanus and diphtheria vaccine. There is no lifelong immunity after a clinical episode of pertussis.

CLINICAL FEATURES

Clinical features in adults are those of the common cold, but after 1 week, prolonged, paroxysmal, and sleep-disturbing cough develops. Whooping is uncommon in adults. Consider pertussis in situations of chronic cough >2 weeks in duration. Cough may last for several months. Since pertussis is highly communicable, with an attack rate of about 20% even in the immunized, suspect pertussis if there is contact with other individuals with prolonged cough. Except in the elderly, pertussis in adults is not associated with pneumonia. Clinical or radiologic evidence of pneumonia in adults or the elderly suggests secondary bacterial infection.

DIAGNOSIS

Diagnosis is often clinical, especially during epidemics. Definitive diagnosis is usually by polymerase chain reaction of nasopharyngeal secretions or serologic detection of antibodies. Other causes of respiratory illnesses with prolonged cough include *Mycoplasma, Chlamydophila*, influenza virus, and other respiratory
viruses. In adults, chronic cough can be associated with angiotensin-converting enzyme inhibitors, gastroesophageal reflux, or asthma.

**TREATMENT**

Treatment of pertussis is azithromycin, 500 milligrams PO on day 1 and 250 milligrams PO on days 2 to 5. Trimethoprim-sulfamethoxazole, 160 milligrams/800 milligrams twice a day for 14 days (check renal dosing), is an alternative to those allergic to, or unable to tolerate, macrolides. Treatment is best if started early, in the first week. After that, antibiotic treatment does not alter the duration of cough. Chemoprophylaxis is typically given for household contacts, although the evidence base for such treatment is weak.

**REFERENCES**


27. Cornia PB, Hersh AL, Lipsky BA et al.: Does this coughing adolescent or adult patient have pertussis. *JAMA*. 2010; 204: 890. [PubMed: 20736473]


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**USEFUL WEB RESOURCES**

2. Information regarding acute bronchitis—
http://journal.publications.chestnet.org/data/Journals/CHEST/22039/95S.pdf

3. World Health Organization: Information regarding severe acute respiratory syndrome—
http://www.who.int/csr/sars/en/