Management of acute bronchitis in healthy adults

Eva Aagaard, MD, Ralph Gonzales, MD, MSPH*

Department of Medicine, University of California, San Francisco, 3333 California Street, Box 1211, San Francisco, CA 94118, USA

Acute respiratory infections (ARIs) are the most common infections in humans. ARIs (nonspecific upper respiratory infections, otitis media, sinusitis, pharyngitis, bronchitis, and pneumonia) account for half of acute conditions each year [1], and consistently rank among the top 10 reasons for ambulatory visits in the United States [2–12]. Acute bronchitis episodes represent a significant portion of these illnesses. Data from the National Health Interview Survey suggest that 4% to 5% of all adults experience one or more episodes of acute bronchitis each year [1]. Furthermore, over 90% of acute bronchitis episodes will come to medical attention [1].

Acute bronchitis is a clinical diagnosis applied to otherwise healthy adults with acute respiratory illness of 1 to 3 weeks’ duration. Acute bronchitis usually is distinguished from other ARIs by the predominance of cough, often accompanied by other respiratory and constitutional symptoms, and the absence of findings suggestive of pneumonia. The importance placed on sputum production and wheezing when making the diagnosis of acute bronchitis varies by physician [13–16]. Cough lasting longer than 3 weeks should be considered “persistent” or “chronic” cough [17,18], and is not discussed here because the diagnostic considerations are significantly different than those of acute bronchitis.

This article focuses on acute bronchitis in otherwise healthy individuals, not on patients who have underlying heart or lung disease or immunosuppression, who generally have been excluded from trials evaluating etiology of and treatment for acute bronchitis. The extent to which one can generalize from the data presented herein is unknown.

* Corresponding author.
E-mail address: ralphg@medicine.ucsf.edu (R. Gonzales).
Acute bronchitis: a transient form of asthma

Clinical features of uncomplicated acute bronchitis develop in sequential phases. Acutely, there is direct inoculation of the tracheobronchial epithelium, characterized clinically by variable constitutional symptoms, including fever, malaise, and myalgias. These symptoms usually last 1 to 5 days, depending on the infectious agent. This phase of illness is often indistinguishable from other acute upper respiratory tract infections. Most uncomplicated upper respiratory infections improve substantially within 5 to 7 days [19,20]. In patients for whom the diagnosis of acute bronchitis would be appropriate, however, the acute phase is followed by a second, protracted phase characterized by persistent cough, often accompanied by phlegm production or wheezing. This second phase usually lasts 1 to 3 weeks, and has as its underlying pathophysiology the hypersensitivity of the tracheobronchial epithelium and airway receptors (reactive airway disease).

During the protracted phase, pulmonary function tests (PFTs) are frequently abnormal and do not seem to be related to either the acute cytopathic effects of the infection or the type of infection (bacterial or viral) [21–25]. Vagal-mediated airway hyperresponsiveness has been shown to coincide with repair of the bronchial epithelium [26]. Other mechanisms of bronchial hyperresponsiveness, such as adrenergic-cholinergic tone imbalance and IgE-mediated histamine release, also may be present. PFT abnormalities seem to be common in acute bronchitis, with approximately 40% of patients demonstrating significant abnormalities by forced expiratory volume (FEV1) or histamine challenge [27,28]. PFT abnormalities are usually transient, typically resolving after 2 to 3 weeks, although they may last as long as 2 months [27–29]. Recurrent episodes of “acute bronchitis” may suggest underlying asthma [30,31]. Although undiagnosed asthma should be considered in patients who have acute cough illness, this diagnosis is difficult to establish because bronchial hyperresponsiveness and PFT abnormalities are frequent in patients who have acute bronchitis. Suspicion and work-up for asthma should be reserved for patients with cough lasting longer than 3 weeks [17].

Microbiology of acute bronchitis

Most acute bronchitis cases seem to have a nonbacterial etiology [29,32,33]. Microbiologic study of acute bronchitis, however, similar to community-acquired pneumonia, can identify a pathogen in only 16% to 55% of cases [32,34]. The significant variability in the frequency of isolation of any pathogen and the types of pathogens identified reflects the patients studied, available technology to identify certain viral and atypical pathogens, and the epidemic nature of the agents that cause acute bronchitis. Additionally, noninfectious causes of acute bronchitis also likely represent some of these cases. Occult asthma, allergic, and occupational exposures should be considered, although their prevalence in adults with acute cough illness remains unclear.
Viral bronchitis

Respiratory viruses seem to cause or serve as a copathogen in most cases of acute bronchitis in epidemiologic studies. The specific viruses most frequently associated with acute bronchitis, in order of frequency of occurrence, are influenza, parainfluenza, respiratory syncitial virus (RSV), coronavirus, adenovirus, and rhinoviruses.

Recent studies have demonstrated the importance of RSV as the etiology of ARIs in adults [35,36]. The impact of RSV is greatest in the elderly, particularly those living in long-term care facilities, and those with underlying heart and lung disease and malignancy [37]. Infection among exposed adults is common, with attack rates approaching 50%, particularly in households with children infected with RSV and in institutional settings [24,37]. Most young and middle-aged adults develop asymptomatic or mildly symptomatic disease, often closely resembling influenza [38]. RSV can be associated with more severe clinical disease and significant morbidity, even in otherwise healthy adults [24]. This morbidity seems to be in part secondary to induced airway hyperreactivity.

In the elderly and institutionalized, lower respiratory illness with RSV is common, with most studies reporting rates of pneumonia and death from 10% to 20% and 2% to 5%, respectively [37]. One report of an outbreak on a geriatrics ward found intense coughing and fever in 96% of patients, productive cough in 64%, and evidence of bronchopneumonia in 40% [39]. In this study, it is unclear whether RSV or secondary bacterial infection caused these pneumonias.

Human metapneumovirus (hMPV), a paramyxovirus [33,40], has emerged recently as an important cause of lower respiratory tract illness and acute bronchitis. Human MPV has been detected in children, adults, the elderly, and the immunocompromised in the Netherlands, Australia, North America, the United Kingdom, and Finland [41–45]. In one study, hMPV was second only to RSV as a cause of respiratory tract illness presenting to a university hospital in the Netherlands [45].

Similar to RSV, hMPV is primarily an illness of the winter months, most commonly causing significant illness in young children and immunocompromised and elderly individuals. Studies suggest that 25% to 50% of hMPV-positive patients who have significant respiratory tract illness have underlying disease [46,47]. Among otherwise healthy adults, hMPV likely causes predominantly mild respiratory illness, but may cause a small but significant portion (approximately 3%) of acute respiratory illness requiring medical attention [46–48].

Bacterial bronchitis

When microbiologic studies are performed on select patients who have uncomplicated acute bronchitis in nonoutbreak settings, less than 10% of
patients have a clear bacterial etiology [29,32,33]. *Bordetella pertussis*, *Chlamydia pneumoniae*, and *Mycoplasma pneumoniae* are the only bacterial pathogens that have been established as causes of acute bronchitis. Although studies have reported the presence of *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis* in adults with acute bronchitis, these studies generally failed to exclude patients who had underlying lung disease, failed to distinguish between colonization and infection [49], or did not differentiate adequately patients who had pneumonia from those who had acute bronchitis when determining causative agents [33]. Furthermore, acute viral respiratory infections seem to increase the proliferation of these bacteria among the oropharyngeal flora [50], further complicating the issue of colonization versus infection. Therefore, sputum Gram stain and culture for common bacterial pathogens have no clinical usefulness in patients who have acute bronchitis.

*Mycoplasma pneumoniae* and *C pneumoniae* have been recognized as possible causes of acute bronchitis since the 1980s [51,52]. Attack rates vary highly, reflecting the seasonal, geographic, and epidemic nature of these infections [21,27,33,53–60]. Studies attempting to distinguish these atypical bacterial pathogens from viral etiologies have shown that patients infected with atypical bacterial pathogens tend to present to medical attention much later than those with confirmed viral bronchitis [21,60,61], and are more likely to have wheezing on clinical examination [21]. In several studies, although these pathogens were present by antibody titer or gene amplification, treatment with antibiotics appropriate to atypical pathogens did not change outcome [33,62–65]. This suggests that in acute bronchitis, *C pneumoniae* and *Mycoplasma pneumoniae* may reflect copathogens or inciting factors for secondary infectious processes, rather than the etiologic agent. Alternatively, because patients with atypical bacterial pathogens present late in the course of illness, the acute infectious process may have resolved with only residual reactive airway disease present at the time of presentation for medical care.

*B pertussis* causes acute bronchitis in previously immunized adults. Natural infection and vaccination with whole-cell and acellular vaccines induce protection from infection for a limited time [21,66–71]. Thus, adolescents and adults gradually may become susceptible to infection again. Symptomatic adult pertussis requiring medical attention occurs at a rate of 71 to 507 per 100,000 population per year (0.1%–0.5% of the population per year) [72–76]. This pool of frequently undiagnosed pertussis [77] provides a reservoir for potentially serious infections in young infants who either are unvaccinated or whose vaccinations are not yet fully effective [78].

The gradual decrease in protection against pertussis likely explains part of the wide variation in presenting symptoms in previously immunized adults. Adults with pertussis generally present with persistent cough, with a mean duration of 36 to 48 days [72,75,77,79–82]. When prolonged cough (longer than 1 week) is present, a significant portion of patients will have
B. pertussis infection, with a frequency ranging from 12% to 32% [71,72,74, 75,79,83–88]. Cough is mostly paroxysmal, and often disturbs sleep. Choking or vomiting and whooping can be present, but less commonly than in children or previously unimmunized adults.

Some have suggested that booster pertussis immunizations for adults or adolescents may curb illness in infants [89]. Whole-cell and acellular pertussis vaccines are well tolerated, with primarily local side effects [90–92]. Only one study has assessed the efficacy of acellular (aP) vaccines in adults [93]. Because of the small sample size of the trial, few pertussis cases were reported (n = 12), and no point estimate of efficacy could be given. The incidence of primary pertussis cases was decreased in the aP group (0.8 per 1000 person-years; 95% CI 0.0–2.1), however, compared with the control group (3.7 per 1000 person-years; 95% CI 1.2–6.2). An epidemiologic model has suggested that a high coverage of adults (greater than 85%) would be needed to reduce effectively the number of cases of infant pertussis [94].

Antibiotic therapy does not seem to decrease duration of symptoms for pertussis unless initiated within 7 to 10 days of the onset of illness [95–97]. Macrolide prophylaxis during outbreak situations and after intrafamilial contacts seems effective [77,98], however, and decreases spread of disease [96,97].

**Distinguishing pneumonia from acute bronchitis**

In the absence of significant comorbid conditions or asthma, the primary objective when evaluating patients who have acute cough illness is excluding pneumonia. The prevalence of pneumonia in patient populations presenting with ARIs varies significantly across study populations, ranging from 3% to 10% in most studies [33,99–101]. Cohort studies have identified clinical features useful for determining which patients do not have pneumonia [99,101–104]. The absence of abnormal vital signs (heart rate greater than 100 beats/minute, respiratory rate greater than 24 breaths/minute, oral temperature above 100.5°F) and chest examination (focal consolidation; eg, rales, egophony, fremitus) reduces the likelihood of pneumonia sufficiently to render further diagnostic testing unnecessary [101]. The specificity (67%–76%), but not sensitivity (62%–71%), of these clinical prediction rules for radiographic pneumonia exceeded physician judgment in a well-designed validation study of 290 adult patients who had acute cough illness [100]. Notably absent from these decision rules is the presence or absence of purulent sputum because purulence (by itself) is a poor predictor of bacterial infections [105,106].

Applying the pneumonia clinical prediction rules should help inform the decision about ordering a chest radiograph, but cannot substitute for clinical judgment. The pneumonia clinical prediction rules have limited application in
the elderly because they may present with atypical manifestations of pneumonia (and without vital sign or examination abnormalities) [107]. Conversely, during the influenza season many patients will have fever or tachycardia but not pneumonia. As a result, chest radiography often is overused in the elderly and during influenza season. In settings where chest radiography is not available readily (eg, many private office practices or rural locations), patients who have cough illness (particularly elderly) may be prescribed antibiotics to safeguard against missing a case of pneumonia.

**Rapid blood tests for bacterial infections**

**C-reactive protein**

A rapid, office-based diagnostic test that improves sensitivity and specificity of detecting pneumonia could be a valuable addition to the current evaluation strategies for patients who have acute cough illness [108]. European experience with an office-based, rapid c-reactive protein (CRP) test, as well as a recent study conducted in the United States, suggests considerable potential to improve diagnostic and treatment decisions for adults with cough illness [109–117]. CRP synthesis is stimulated in response to many inflammatory conditions, and levels increase preferentially (but not exclusively) by bacterial (versus viral) infections. The serum levels of CRP associated with bacterial infections are 10 to 50 fold higher than those used to predict atherosclerotic heart disease.

Despite widespread use in Europe, and recent US Food and Drug Administration approval of a rapid CRP test in the United States, the role of rapid CRP testing in the management of adults with acute cough illness has not been defined rigorously. Most studies found a high sensitivity (80%–100%), but CRP levels may lack the specificity (60%–70%) necessary to diagnose bacterial infections in isolation. Integrating CRP testing into a clinical algorithm is one strategy to improve its specificity while taking advantage of its sensitivity for detecting acute bacterial infections such as pneumonia. Future studies assessing the effectiveness of a CRP-based clinical algorithm are necessary.

**Procalcitonin**

Recent studies of procalcitonin in serum also have shown levels to distinguish bacterial from viral illnesses [118,119]. Early procalcitonin assays had a limited functional assay sensitivity (0.3–0.5 µg/L), and therefore were not accurate for the diagnosis of early or localized infections [120,121]. A newer assay with improved functional sensitivity (0.06 µg/L) has become available in Europe, however. One recent study adopting a test-based clinical algorithm with this rapid procalcitonin testing among adults admitted to the hospital with lower respiratory tract infection demonstrated a large reduction in antibiotic use, and equivalent outcomes [122].
Acute bronchitis and antibiotics

Should antibiotics ever be used?

Antibiotic prescription rates for acute bronchitis range from 50% to 80% in studies from multiple settings and countries [123–125]. Studies have failed to show any meaningful benefit from antibiotics in the treatment of acute bronchitis, however. Systematic reviews and meta-analyses of nine randomized placebo-controlled trials conducted between 1970 and 2000 conclude that routine antibiotic treatment of acute bronchitis has no consistent effect on either the duration or severity of illness. In one meta-analysis, there was no significant impact on the duration of cough [126], but two other meta-analyses reported a small but statistically significant decrease in cough duration (one third days fewer of cough after 7 days) associated with treatment with antibiotics [127,128]. In all three meta-analyses, there was no significant impact on overall illness duration, activity limitation, or work loss. A recent randomized, double-blind, controlled study comparing azithromycin with vitamin C has addressed concerns that the earlier trials were performed with older antibiotics, some of which had no activity against the atypical agents implicated in acute bronchitis [129]. This study found no advantage to antibiotic treatment on illness outcomes or return-to-work status.

As discussed earlier, antibiotic prescription is appropriate when the physician suspects pertussis infection. Antibiotics should be reserved for adults exposed to known pertussis infection, or to patients who have acute bronchitis in the setting of a documented pertussis epidemic. Although antibiotics do not decrease the duration of illness in this setting, they can decrease bacterial shedding and spread. Antibiotics also may be considered in the setting of a known mycoplasma or C pneumoniae outbreak, although data are lacking on their effectiveness in this setting.

The harm of overusing antibiotics

The societal cost of inappropriate antibiotic use is the rapid emergence of antibiotic resistance among bacterial pathogens [130–132]. Resistance is rising among common community-acquired pathogens, including S pneumoniae (DRSP) [133–135]. This pathogen is a leading cause of ear and sinus infections, pneumonia, sepsis, and meningitis in the United States. At the community level, the mean increase in DRSP prevalence is directly proportional to the amount of antibiotics consumed [136]. On an individual level, a person’s risk for carriage, transmission, and invasive infection with antibiotic-resistant bacteria is associated strongly with prior antibiotic use [137–140].

Finally, the sheer magnitude of antibiotic prescriptions dispensed each year for ARIs requires that excess health care costs also be considered. In 1998, 41 million antibiotic prescriptions were written for ARIs, 55% of
which were likely unnecessary [141]. The cost of these excess prescriptions was estimated at $726 million. Similar high rates of inappropriate antibiotic use are seen in Europe [142]. In addition, the result of antibiotic resistance on antibiotic selection and clinical outcomes further increases health care costs [143].

*If they don’t work, why are antibiotics so frequently prescribed for acute bronchitis?*

Physician education likely reflects a small component of inappropriate antibiotic use. Evidence suggests that physicians and patients are more likely to believe that antibiotics are appropriate if purulent secretions are present [144,145], despite significant evidence to the contrary. Physician specialty and level of training also are associated with antibiotic prescriptions for ARIs. Family medicine physicians are more likely to prescribe antibiotics to children with ARIs than pediatricians [146]. Also, providers that are further from medical school graduation and practicing in rural areas are more likely to prescribe antibiotics [147].

Antibiotic prescribing behavior is associated poorly with clinicians’ subjective norms and intentions, which suggests that external forces such as patient-specific beliefs and health plan factors play a greater role [148] than physician knowledge. Patients frequently expect to receive antibiotics for uncomplicated acute bronchitis [149,150] and patients or parents who expect antibiotics are more likely to receive them [150,151]. Communication elements associated with antibiotic prescriptions for ARIs include patient appeals to specific life circumstances (eg, a pressing social engagement), identification of a previous positive experience with antibiotic use [81], or being labeled as having “acute bronchitis” rather than a “chest cold” [149].

Not surprisingly, clinicians with greater patient workloads prescribe antibiotics for ARIs more frequently, likely reflecting the perceived time it would take to discuss the inappropriateness of antibiotic use in ARIs [152]. Other health plan factors that may contribute to prescribing behavior include restricting formularies and practice characteristics such as payment structure. A recent survey of physicians’ attitudes regarding the role of societal risks in making antibiotic treatment decisions for individual patients found that societal concerns about promoting antibiotic resistance ranked below patient-centered factors such as ease of use and cost to the patient [153].

Despite physician concerns about patient expectations, most studies find that satisfaction with care for ARIs is tied more closely to how much time the physician spent explaining the illness, rather than receipt of antibiotics [150,151,154]. Communication elements associated with high patient satisfaction include positive responses to the following statements: “the doctor spent enough time with me”; “the doctor explained the illness to me”; and “the doctor treated me with respect” [147]. An intervention
strategy consisting of patient and clinician education reduced antibiotic prescription rates for acute bronchitis in adults [155], but did not decrease patient satisfaction [147]. Furthermore, antibiotic prescribing does not seem to reduce additional care seeking in adult patients [156].

Nonantibiotic treatment of acute bronchitis

Anti-influenzal therapy

Influenza is the most common cause of acute bronchitis, and influenza vaccination is the most effective strategy for preventing influenzal illness. Treatment for high-risk exposed individuals and those who present within 48 hours of symptom onset is also possible. Amantadine, rimantidine, zanamivir, and oseltamivir decrease illness duration by approximately 1 day and lead to a 0.5-day quicker return to normal activities [157]. The primary difference between the agents is that the neuraminidase inhibitors are effective against influenza A and B, whereas amantadine and rimantidine are effective only against influenza A. The relative proportion of cases caused by each type of influenza virus varies from year to year, and is determined best through consultation with local public health agencies. Adverse events are modestly more common with rimantidine (32% of patients, most commonly central nervous system) than with the neuraminidase inhibitors (24% of patients, mostly gastrointestinal) [157]. Because each of these therapies is only effective if initiated within the first 48 hours, and preferably 30 hours, of symptom onset, rapid diagnosis is key. During documented influenza outbreaks, the positive predictive value of clinical diagnosis based on clinician judgment is good (correct approximately 70% of the time) [158], and compares favorably with rapid diagnostic tests for influenza (sensitivities of 63%–81%) [158–160]. Diagnosis of influenza in a nonoutbreak period is more difficult and diagnostic testing should be considered.

Antiviral treatment for other viral illness either have been studied inadequately, carry inappropriately high side-effect profiles, or are ineffective in otherwise healthy individuals [161]. Ribavirin is indicated in bone marrow transplant patients who have RSV, and in this population reduces morbidity and mortality [162].

Bronchodilator therapy

Three randomized, controlled trials have demonstrated a consistent benefit to bronchodilator treatment [163–165]. Approximately 50% fewer patients report the presence of cough after 7 days of treatment. This benefit seems to be greatest in the subset of patients who had bronchial hyperresponsiveness. A large trial of patients who had URI-associated cough, but not clearly acute bronchitis, reported no benefit of bronchodilator treatment [166]. A meta-analysis of these studies showed no significant
benefit from b2-agonists [167], but is limited by the addition of the Littenberg study, which enrolled patients who had acute, nonspecific cough. Whether anticholinergic bronchodilator therapy is effective in patients who have uncomplicated acute bronchitis is not known. Similarly, no studies have examined the effect of inhaled corticosteroid therapy, although the delay in onset of action for this type of therapy (1–2 weeks) may preclude finding a major benefit.

antitussive therapy

The effectiveness of antitussive therapy seems to depend on the cause of cough illness. Acute or early cough caused by colds and other upper respiratory tract infections does not seem to respond to dextromethorphan or codeine. Cough of greater than 3 weeks’ duration, cough associated with underlying lung disease, and experimentally induced cough seem to respond to these agents. Given that the cough of acute bronchitis often lasts for 2 to 3 weeks, these agents likely have a modest impact on cough severity and duration.

immunomodulating therapies

Most trials of immunomodulatory (alternative) therapies have been conducted on patients who have early symptoms of colds and nonspecific ARIs. As a result, these data are difficult to extrapolate to patients who have acute bronchitis, who generally present later and with more severe illness. Vitamin C at doses exceeding 1 g/d seems to offer small but significant reduction in illness duration of about 0.5 day per cold episode [168]. Well-performed clinical trials comprising mostly small studies of zinc gluconate and zinc acetate lozenges have had mixed results [169] and their benefit is unclear. Echinacea seems to be of benefit in some preparations [170], but there is significant heterogeneity of study design, as well as preparations tested. Also, quality control of echinacea preparations sold to the community is poor, with one study demonstrating that 10% of single-herb echinacea preparations in one metropolitan area had no active ingredient, and less than half met the quality standards described on the label [171].

A recent randomized, double-blind, placebo-controlled trial has shown the benefit of an extract of *Pelargonium sidoides* roots in acute bronchitis [172]. This plant extract is used commonly in Europe and Mexico. Its mechanism of action is poorly understood, but is believed to be immunomodulatory in nature, having been used first in the early 1900s as a treatment for tuberculosis. In the recent study, adult patients who had acute bronchitis of greater than 48 hours’ duration and a bronchial severity score (BSS) of at least 5 points were enrolled. Patients were excluded if they were to receive or recently had received antibiotics or had other serious illnesses. Patients were randomized to receive active ingredient or color-, smell-, viscosity-, and taste-matched placebo. Among patients receiving pelargonium, decrease in BSS on
day 7 was 5.9 points compared with 3.2 points for placebo ($P < .0001$). Duration of illness ($P < .001$) and inability to work (16% versus 43%, $P < .0001$) were significantly less in the pelargonium group compared with placebo. Further studies are necessary to confirm these interesting results. In the United States, *Pelargonium sidoides* is marketed under the trade name Umcka (Nature’s Way, Springville, Utah).

**Approach to the patient with acute bronchitis**

The approach to the otherwise healthy patient with acute cough illness first should be to assess his or her likelihood of pneumonia. In the nonelderly patient without abnormal vital signs or consolidative lung findings, the likelihood of pneumonia is less than 1% in the ambulatory care setting [99,101]. When these abnormalities are present, a chest radiograph should be considered, depending on overall clinical impression and likelihood of influenza. For patients who present with prolonged cough (longer than 1 week), pertussis should be considered, along with bronchial hyperresponsiveness.

Once a diagnosis of acute bronchitis has been made, providers should address symptomatic treatment and patient expectations for the visit. Physicians should validate the severity of the patient’s illness (because it has affected the patient’s activities enough to seek care and acute bronchitis significantly decreases quality of life) [173]. Treatment discussions should focus on alleviating symptoms and providing realistic expectations for the duration of symptoms. Patients should be informed that they should expect their cough to last 10 to 14 days after the office visit. Providers should also inform patients of which symptoms should prompt a return to the clinic or office.

For patients who request antibiotics for clear viral infections, providers should discuss the lack of benefit and the risks of inappropriate antibiotic use. These risks should be personalized as much as possible, informing them that previous antibiotic use increases their personal risk of carriage and infection with antibiotic-resistant infections. In addition, antibiotics cause frequent side effects, especially of the gastrointestinal tract.

Symptomatic treatment will depend on severity of illness and time at presentation. Alternative and over-the-counter preparations may be most effective in the early stages of illness. For those with prolonged or severe cough or clear bronchial hyperresponsiveness, bronchodilator treatment and antitussives should be considered. Further studies are necessary on the plant extract *Pelargonium sidoides* to assess further its benefit in this setting.

**References**

[1] Benson V, Marano MA. Current estimates from the National Health Interview Survey, 1995. Vital Health Stat 10 1998;199:1–428.
[2] Cherry DK, Burt CW, Woodwell DA. National Ambulatory Medical Care Survey: 2001 summary. Adv Data 2003;337:1–44.
[3] Cherry DK, Woodwell DA. National Ambulatory Medical Care Survey: 2000 summary. Adv Data 2002;328:1–32.
[4] Schappert SM. National Ambulatory Medical Care Survey: 1989 summary. Vital Health Stat 13 1992;1–80.
[5] Schappert SM. National Ambulatory Medical Care Survey: 1990 summary. Adv Data 1992;1–11.
[6] Schappert SM. National Ambulatory Medical Care Survey: 1991 summary. Adv Data 1993;1–16.
[7] Schappert SM. National Ambulatory Medical Care Survey: 1992 summary. Adv Data 1994;1–20.
[8] Schappert SM. National Ambulatory Medical Care Survey: 1994 summary. Adv Data 1996;1–18.
[9] Woodwell DA. National Ambulatory Medical Care Survey: 1995 summary. Adv Data 1997;1–25.
[10] Woodwell DA. National Ambulatory Medical Care Survey: 1996 summary. Adv Data 1997;1–25.
[11] Woodwell DA. National Ambulatory Medical Care Survey: 1997 summary. Adv Data 1999;1–28.
[12] Woodwell DA, Schappert SM. National Ambulatory Medical Care Survey: 1993 summary. Adv Data 1995;1–20.
[13] Kawamoto R, Asai Y, Nago N, et al. A study of clinical features and treatment of acute bronchitis by Japanese primary care physicians. Fam Pract 1998;15:244–51.
[14] Leiner S. Acute bronchitis in adults: commonly diagnosed but poorly defined. Nurse Pract 1997;22:104,107–8,113–7.
[15] Oeffinger KC, Snell LM, Foster BM, et al. Diagnosis of acute bronchitis in adults: a national survey of family physicians. J Fam Pract 1997;45:202–9.
[16] Stocks N, Fahey T. Labeling of acute respiratory illness: evidence of between-practitioner variation in the UK. Fam Pract 2002;19:375–7.
[17] Irwin RS, Boulet LP, Cloutier MM, et al. Managing cough as a defense mechanism and as a symptom. A consensus panel report of the American College of Chest Physicians. Chest 1998;114:133S–81S.
[18] Irwin RS, Madison JM. The diagnosis and treatment of cough. N Engl J Med 2000;343:1715–21.
[19] Heikkinen T, Jarvinen A. The common cold. Lancet 2003;361:51–9.
[20] Puhakka T, Makela MJ, Malmstrom K, et al. The common cold: effects of intranasal fluticasone propionate treatment. J Allergy Clin Immunol 1998;101:726–31.
[21] Hahn DL, Dodge RW, Golubiatnikov R. Association of Chlamydia pneumoniae (strain TWAR) infection with wheezing, asthmatic bronchitis, and adult-onset asthma. JAMA 1991;266:225–30.
[22] Hall WJ, Douglas RG Jr. Pulmonary function during and after common respiratory infections. Annu Rev Med 1980;31:233–8.
[23] Hall WJ, Hall CB. Clinical significance of pulmonary function tests. Alterations in pulmonary function following respiratory viral infection. Chest 1979;76:458–65.
[24] Hall WJ, Hall CB, Speers DM. Respiratory syncytial virus infection in adults: clinical, virologic, and serial pulmonary function studies. Ann Intern Med 1978;88:203–5.
[25] Little JW, Hall WJ, Douglas RG Jr, et al. Airway hyperreactivity and peripheral airway dysfunction in influenza A infection. Am Rev Respir Dis 1978;118:295–303.
[26] Polito AJ, Proud D. Epithelia cells as regulators of airway inflammation. J Allergy Clin Immunol 1998;102:714–8.
[27] Boldy DA, Skidmore SJ, Ayres JG. Acute bronchitis in the community: clinical features, infective factors, changes in pulmonary function and bronchial reactivity to histamine. Respir Med 1990;84:377–85.
[28] Williamson HA Jr. Pulmonary function tests in acute bronchitis: evidence for reversible airway obstruction. J Fam Pract 1987;25:251–6.
[29] Melbye H, Kongerud J, Vorland L. Reversible airflow limitation in adults with respiratory infection. Eur Respir J 1994;7:1239–45.
[30] Hallett JS, Jacobs RL. Recurrent acute bronchitis: the association with undiagnosed bronchial asthma. Ann Allergy 1985;55:568–70.
[31] Williamson HA Jr, Schultz P. An association between acute bronchitis and asthma. J Fam Pract 1987;24:35–8.
[32] Gonzales R, Bartlett JG, Besser RE, et al. Principles of appropriate antibiotic use for treatment of uncomplicated acute bronchitis: background. Ann Emerg Med 2001;37:720–7.
[33] Macfarlane J, Holmes W, Gard P, et al. Prospective study of the incidence, aetiology and outcome of adult lower respiratory tract illness in the community. Thorax 2001;56:109–14.
[34] Jonsson JS, Sigurdsson JA, Kristinsson KG, et al. Acute bronchitis in adults. How close do we come to its aetiology in general practice? Scand J Prim Health Care 1997;15:156–60.
[35] Falsey AR, Walsh EE. Respiratory syncytial virus infection in adults. Clin Microbiol Rev 2000;13:371–84.
[36] Treanor J, Falsey A. Respiratory viral infections in the elderly. Antiviral Res 1999;44:79–102.
[37] Greenberg SB. Respiratory viral infections in adults. Curr Opin Pulm Med 2002;8:201–8.
[38] Zambon MC, Stockton JD, Clewley JP, et al. Contribution of influenza and respiratory syncytial virus to community cases of influenza-like illness: an observational study. Lancet 2001;358:1410–6.
[39] Agius G, Dindinaud G, Biggar RJ, et al. An epidemic of respiratory syncytial virus in elderly people: clinical and serological findings. J Med Virol 1990;30:117–27.
[40] van den Hoogen BG, de Jong JC, Groen J, et al. A newly discovered human pneumovirus isolated from young children with respiratory tract disease. Nat Med 2001;7:719–24.
[41] Nissen MD, Siebert DJ, Mackay IM, et al. Evidence of human metapneumovirus in Australian children. Med J Aust 2002;176:188.
[42] Pelletier G, Dery P, Abed Y, et al. Respiratory tract re-infections by the new human Metapneumovirus in an immunocompromised child. Emerg Infect Dis 2002;8:976–8.
[43] Peret TC, Boivin G, Li Y, et al. Characterization of human metapneumoviruses isolated from patients in North America. J Infect Dis 2002;185:1660–3.
[44] Stockton J, Stephenson I, Fleming D, et al. Human metapneumovirus as a cause of community-acquired respiratory illness. Emerg Infect Dis 2002;8:897–901.
[45] van den Hoogen BG, van Doornum GJ, Fockens JC, et al. Prevalence and clinical symptoms of human metapneumovirus infection in hospitalized patients. J Infect Dis 2003;188:1571–7.
[46] Boivin G, Abed Y, Pelletier G, et al. Virological features and clinical manifestations associated with human metapneumovirus: a new paramyxovirus responsible for acute respiratory-tract infections in all age groups. J Infect Dis 2002;186:1330–4.
[47] van den Hoogen BG, Osterhaus DM, Fouchier RA. Clinical impact and diagnosis of human metapneumovirus infection. Pediatr Infect Dis J 2004;23:S25–32.
[48] Falsey AR, Erdman D, Anderson LJ, et al. Human metapneumovirus infections in young and elderly adults. J Infect Dis 2003;187:785–90.
[49] Ramirez-Ronda CH, Fuxench-Lopez Z, Nevarez M. Increased pharyngeal bacterial colonization during viral illness. Arch Intern Med 1981;141:1599–603.
[50] Brimblecombe FS, Cruickshank R, Masters PL, et al. Family studies of respiratory infections, Br Med J 1958;29:119–28.
[51] Cassell GH, Cole BC. Mycoplasmas as agents of human disease. N Engl J Med 1981;304:80–9.
[52] Grayston JT, Kuo CC, Wang SP, et al. A new Chlamydia psittaci strain, TWAR, isolated in acute respiratory tract infections. N Engl J Med 1986;315:161–8.
[53] Blasi F, Centanni S, Allegra L. Chlamydia pneumoniae: crossing the barriers? Eur Respir J 2004;23:499–500.
[54] Falck G, Heyman L, Gnarpe J, et al. Chlamydia pneumoniae (TWAR): a common agent in acute bronchitis. Scand J Infect Dis 1994;26:179–87.
[55] Grayston JT, Aldous MB, Easton A, et al. Evidence that Chlamydia pneumoniae causes pneumonia and bronchitis. J Infect Dis 1993;168:1231–5.
[56] Jantos C, Artelt P, Schiefer HG. Acute lower respiratory tract infection associated with Chlamydia pneumoniae in Germany. Eur J Clin Microbiol Infect Dis 1993;12:33–5.
[57] Lieberman D, Shvartzman P, Lieberman D, et al. Etiology of respiratory tract infection in adults in a general practice setting. Eur J Clin Microbiol Infect Dis 1998;17:685–9.
[58] Mordhorst CH, Wang SP, Grayston JT. Outbreak of Chlamydia pneumoniae infection in four farm families. Eur J Clin Microbiol Infect Dis 1992;11:617–20.
[59] Tannock GA, Reid AL, Gillett SM, et al. A study of respiratory infections in a healthy adult population during the 1987 Australian winter. Fam Pract 1993;10:378–86.
[60] Thom DH, Grayston JT, Campbell LA, et al. Respiratory infection with Chlamydia pneumoniae in middle-aged and older adult outpatients. Eur J Clin Microbiol Infect Dis 1994;13:785–92.
[61] Wright SW, Edwards KM, Decker MD, et al. Prevalence of positive serology for acute Chlamydia pneumoniae infection in emergency department patients with persistent cough. Acad Emerg Med 1997;4:179–83.
[62] File TM Jr, Segreti J, Dunbar L, et al. A multicenter, randomized study comparing the efficacy and safety of intravenous and/or oral levofloxacin versus ceftriaxone and/or cefuroxime axetil in treatment of adults with community-acquired pneumonia. Antimicrob Agents Chemother 1997;41:1965–72.
[63] Kauppinen MT, Saikku P, Kujala P, et al. Clinical picture of community-acquired Chlamydia pneumoniae pneumonia requiring hospital treatment: a comparison between chlamydial and pneumococcal pneumonia. Thorax 1996;51:185–9.
[64] King DE, Williams WC, Bishop L, et al. Effectiveness of erythromycin in the treatment of acute bronchitis. J Fam Pract 1996;42:601–5.
[65] Macfarlane J, Prewett J, Rose D, et al. Prospective case-control study of role of infection in patients who reconsult after initial antibiotic treatment for lower respiratory tract infection in primary care. Br Med J 1997;315:1206–10.
[66] Grimpel E, Begue P, Anjak I, et al. Long-term human serum antibody responses after immunization with whole-cell pertussis vaccine in France. Clin Diagn Lab Immunol 1996;3:93–7.
[67] He Q, Viljanen MK, Nikkari S, et al. Outcomes of Bordetella pertussis infection in different age groups of an immunized population. J Infect Dis 1994;170:873–7.
[68] Jenkinson D. Duration of effectiveness of pertussis vaccine: evidence from a 10 year community study. BMJ (Clin.Res Ed) 1988;296:612–4.
[69] Lugauer S, Heininger U, Cherry JD, et al. Long-term clinical effectiveness of an acellular pertussis component vaccine and a whole cell pertussis component vaccine. Eur J Pediatr 2002;161:142–6.
[70] Salmaso S, Mastrantonio P, Tozzi AE, et al. Sustained efficacy during the first 6 years of life of 3-component acellular pertussis vaccines administered in infancy: the Italian experience. Pediatrics 2001;108:E81.
[71] Wirsing von Konig CH, Postels-Multanis S, Bock HL, et al. Pertussis in adults: frequency of transmission after household exposure. Lancet 1995;346:1326–9.
[72] Gilberg S, Njamkepo E, Du C, et al. Evidence of Bordetella pertussis infection in adults presenting with persistent cough in a French area with very high whole-cell vaccine coverage. J Infect Dis 2002;186:415–8.
Guris D, Strebel PM, Bardenheier B, et al. Changing epidemiology of pertussis in the United States: increasing reported incidence among adolescents and adults, 1990–1996. Clin Infect Dis 1999;28:1230–7.

Miller E, Fleming DM, Ashworth LA, et al. Serological evidence of pertussis in patients presenting with cough in general practice in Birmingham. Commun Dis Public Health 2000;3:132–4.

Strebel P, Nordin J, Edwards K, et al. Population-based incidence of pertussis among adolescents and adults, Minnesota, 1995–1996. J Infect Dis 2001;183:1353–9.

Yih WK, Lett SM, des Vignes FN, et al. The increasing incidence of pertussis in Massachusetts adolescents and adults, 1989–1998. J Infect Dis 2000;182:1409–16.

De Serres G, Shadmani R, Duval B, et al. Morbidity of pertussis in adolescents and adults. J Infect Dis 2000;182:174–9.

Baron S, Njamkepo E, Grimprel E, et al. Epidemiology of pertussis in French hospitals in 1993 and 1994: thirty years after a routine use of vaccination. Pediatr Infect Dis J 1998;17:412–8.

Birkebaek NH, Kristiansen M, Seefeldt T, et al. Bordetella pertussis and chronic cough in adults. Clin Infect Dis 1999;29:1239–42.

Postels-Multani S, Schmitt HJ, Wirsing von Konig CH, et al. Symptoms and complications of pertussis in adults. Infection 1995;23:139–42.

Scott JG, Cohen D, DiCicco-Bloom B, et al. Antibiotic use in acute respiratory infections and the ways patients pressure physicians for a prescription. J Fam Pract 2001;50:853–8.

Trollfors B. Effect of erythromycin and amoxycillin on Bordetella pertussis in the nasopharynx. Infection 1978;6:228–30.

Mink CM, Cherry JD, Christenson P, et al. A search for Bordetella pertussis infection in university students. Clin Infect Dis 1992;14:464–71.

Robertson PW, Goldberg H, Jarvie BH, et al. Bordetella pertussis infection: a cause of persistent cough in adults. Med J Aust 1987;146:522–5.

Rosenthal S, Strebel P, Cassiday P, et al. Pertussis infection among adults during the 1993 outbreak in Chicago. J Infect Dis 1995;171:1650–2.

Schmitt-Grohe S, Cherry JD, Heininger U, et al. Pertussis in German adults. Clin Infect Dis 1995;21:860–6.

Senzilet LD, Halperin SA, Spika JS, et al. Pertussis is a frequent cause of prolonged cough illness in adults and adolescents. Clin Infect Dis 2001;32:1691–7.

Wright SW, Edwards KM, Decker MD, et al. Pertussis seroprevalence in emergency department staff. Ann Emerg Med 1994;24:413–7.

Campins-Marti M, Cheng HK, Forsyth K, et al. Recommendations are needed for adolescent and adult pertussis immunisation: rationale and strategies for consideration. Vaccine 2001;20:641–6.

Granstrom M, Thoren M, Blennow M, et al. Acellular pertussis vaccine in adults: adverse reactions and immune response. Eur J Clin Microbiol 1987;6:18–21.

Keitel WA, Muenz LR, Decker MD, et al. A randomized clinical trial of acellular pertussis vaccines in healthy adults: dose-response comparisons of 5 vaccines and implications for booster immunization. J Infect Dis 1999;180:397–403.

Storsaeter J, Blackwelder WC, Hallander HO. Pertussis antibodies, protection, and vaccine efficacy after household exposure. Am J Dis Child 1992;146:167–72.

Ward J, Partridge S, Chang S, et al. Acellular pertussis vaccine efficacy and epidemiology of pertussis in adolescents and adults: NIH multicenter adult pertussis trial (APERT). Bethesda (MD): National Institutes of Health; 2000.

Hethcote HW. Simulations of pertussis epidemiology in the United States: effects of adult booster vaccinations. Math Biosci 1999;158:47–73.

Bergquist SO, Bernander S, Dahnsjo H, et al. Erythromycin in the treatment of pertussis: a study of bacteriologic and clinical effects. Pediatr Infect Dis J 1987;6:458–61.
[96] Sprauer MA, Cochi SL, Zell ER, et al. Prevention of secondary transmission of pertussis in households with early use of erythromycin. Am J Dis Child 1992;146:177–81.
[97] Wirsing von Konig CH, Postels-Multani S, Bogaerts H, et al. Factors influencing the spread of pertussis in households. Eur J Pediatr 1998;157:391–4.
[98] Steketee RW, Wassilak SG, Adkins WN Jr, et al. Evidence for a high attack rate and efficacy of erythromycin prophylaxis in a pertussis outbreak in a facility for the developmentally disabled. J Infect Dis 1988;157:434–40.
[99] Diehr P, Wood RW, Bushyhead J, et al. Prediction of pneumonia in outpatients with acute cough—a statistical approach. J Chronic Dis 1984;37:215–25.
[100] Emerman CL, Dawson N, Speroff T, et al. Comparison of physician judgment and decision aids for ordering chest radiographs for pneumonia in outpatients. Ann Emerg Med 1991;20:1215–9.
[101] Metlay JP, Kapoor WN, Fine MJ. Does this patient have community-acquired pneumonia? Diagnosing pneumonia by history and physical examination. JAMA 1997;278:1440–5.
[102] Gennis P, Gallagher J, Falvo C, et al. Clinical criteria for the detection of pneumonia in adults: guidelines for ordering chest radiographs in the emergency department. J Emerg Med 1989;7:263–8.
[103] Heckerling PS, Tape TG, Wigton RS, et al. Clinical prediction rule for pulmonary infiltrates. Ann Intern Med 1990;113:664–70.
[104] Singal BM, Hedges JR, Radack KL. Decision rules and clinical prediction of pneumonia: evaluation of low-yield criteria. Ann Emerg Med 1989;18:13–20.
[105] Gerberding JL. Sputum aeruginosa: time to rewrite the textbooks on virus-induced airway inflammation. Am J Med 2000;108:91–2.
[106] Kaiser L, Lew D, Hirschel B, et al. Effects of antibiotic treatment in the subset of common-cold patients who have bacteria in nasopharyngeal secretions. Lancet 1996;347:1507–10.
[107] Metlay JP, Schulz R, Li YH, et al. Influence of age on symptoms at presentation in patients with community-acquired pneumonia. Arch Intern Med 1997;157:1453–9.
[108] Metlay JP, Fine MJ. Testing strategies in the initial management of patients with community-acquired pneumonia. Ann Intern Med 2003;138:109–18.
[109] Albazzaz MK, Pal C, Berman P, et al. Inflammatory markers of lower respiratory tract infection in elderly people. Age Ageing 1994;23:299–302.
[110] Almirall J, Bolibar I, Toran P, et al. Contribution of C-reactive protein to the diagnosis and assessment of severity of community-acquired pneumonia. Chest 2004;125:1335–42.
[111] Flanders SA, Stein J, Shochat G, et al. Performance of a bedside C-reactive protein test in the diagnosis of community-acquired pneumonia in adults with acute cough. Am J Med 2004;116:529–35.
[112] Garcia VE, Martinez JA, Mensa J, et al. C-reactive protein levels in community-acquired pneumonia. Eur Respir J 2003;21:702–5.
[113] Hopstaken RM, Muris JW, Knottnerus JA, et al. Contributions of symptoms, signs, erythrocyte sedimentation rate, and C-reactive protein to a diagnosis of pneumonia in acute lower respiratory tract infection. Br J Gen Pract 2003;53:358–64.
[114] Ortgvist A, Hedlund J, Wretlind B, et al. Diagnostic and prognostic value of interleukin-6 and C-reactive protein in community-acquired pneumonia. Scand J Infect Dis 1995;27:457–62.
[115] Requejo HI, Coozca AM. C-reactive protein in the diagnosis of community-acquired pneumonia. Braz J Infect Dis 2003;7:241–4.
[116] Smith RP, Lipworth BJ. C-reactive protein in simple community-acquired pneumonia. Chest 1995;107:1028–31.
[117] Smith RP, Lipworth BJ, Cree IA, et al. C-reactive protein. A clinical marker in community-acquired pneumonia. Chest 1995;108:1288–91.
[118] Assicot M, Gendrel D, Carsin H, et al. High serum procalcitonin concentrations in patients with sepsis and infection. Lancet 1993;341:515–8.
[119] Muller B, Becker KL, Schachinger H, et al. Calcitonin precursors are reliable markers of sepsis in a medical intensive care unit. Crit Care Med 2000;28:977–83.
[120] Kurzai W, Oberhoffer M, Meier-Hellmann A, et al. Procalcitonin—a new indicator of the systemic response to severe infections. Infection 1997;25:329–34.
[121] Nylen E, Muller B, Becker KL, et al. The future diagnostic role of procalcitonin levels: the need for improved sensitivity. Clin Infect Dis 2003;36:823–4.
[122] Christ-Crain M, Jaecd-Morning D, Bingisser R, et al. Effect of procalcitonin-guided treatment on antibiotic use and outcome in lower respiratory tract infections: cluster-randomised, single-blinded intervention trial. Lancet 2004;363:600–7.
[123] Gonzales R, Steiner JF, Sande MA. Antibiotic prescribing for adults with colds, upper respiratory tract infections, and bronchitis by ambulatory care physicians. JAMA 1997;278:901–4.
[124] Meza RA, Bridges-Webb C, Sayer GP, et al. The management of acute bronchitis in general practice: results from the Australian Morbidity and Treatment Survey, 1990–1991. Aust Fam Physician 1994;23:150–3.
[125] Verheij TJ, Hermans J, Kaptein AA, et al. Acute bronchitis: general practitioners’ views regarding diagnosis and treatment. Fam Pract 1990;7:175–80.
[126] Fahey T, Stocks N, Thomas T. Quantitative systematic review of randomised controlled trials comparing antibiotic with placebo for acute cough in adults. BMJ 1998;316:906–10.
[127] Becker L, Glazier R, McIsaac W, et al. Antibiotics for acute bronchitis. Cochrane Database Syst Rev 2000;CD000245.
[128] Bent S, Saint S, Vittinghoff E, et al. Antibiotics in acute bronchitis: a meta-analysis. Am J Med 1999;107:62–7.
[129] Evans AT, Husain S, Durairaj L, et al. Azithromycin for acute bronchitis: a randomised, double-blind, controlled trial. Lancet 2002;359:1648–54.
[130] Kunin CM. Resistance to antimicrobial drugs—a worldwide calamity. Ann Intern Med 1993;118:557–61.
[131] Lederberg J. Infectious disease—a threat to global health and security. JAMA 1996;276:417–9.
[132] Levy SB. Confronting multidrug resistance. A role for each of us. JAMA 1993;269:1840–2.
[133] Chen DK, McGeer A, de Azavedo JC, et al. Decreased susceptibility of Streptococcus pneumoniae to fluoroquinolones in Canada. Canadian Bacterial Surveillance Network. N Engl J Med 1999;341:233–9.
[134] Doern GV, Brueggemann AB, Huynh H, et al. Antimicrobial resistance with Streptococcus pneumoniae in the United States, 1997–98. Emerg Infect Dis 1999;5:757–65.
[135] Whitney CG, Farley MM, Hadler J, et al. Increasing prevalence of multidrug-resistant Streptococcus pneumoniae in the United States. N Engl J Med 2000;343:1917–24.
[136] Diekema DJ, Brueggemann AB, Doern GV. Antimicrobial-drug use and changes in resistance in Streptococcus pneumoniae. Emerg Infect Dis 2000;6:552–6.
[137] Hofmann J, Cetron MS, Farley MM, et al. The prevalence of drug-resistant Streptococcus pneumoniae in Atlanta. N Engl J Med 1995;333:481–6.
[138] Moreno F, Crisp C, Jorgensen JH, et al. The clinical and molecular epidemiology of bacteremias at a university hospital caused by pneumococci not susceptible to penicillin. J Infect Dis 1995;172:427–32.
[139] Nava JM, Bella F, Garau J, et al. Predictive factors for invasive disease due to penicillin-resistant Streptococcus pneumoniae: a population-based study. Clin Infect Dis 1994;19:884–90.
[140] Nuorti JP, Butler JC, Crutcher JM, et al. An outbreak of multidrug-resistant pneumococcal pneumonia and bacteremia among unvaccinated nursing home residents. N Engl J Med 1998;338:1861–8.
[141] Gonzales R, Malone DC, Maselli JH, et al. Excessive antibiotic use for acute respiratory infections in the United States. Clin Infect Dis 2001;33:757–62.
[142] Cars O, Molstad S, Melander A. Variation in antibiotic use in the European Union. Lancet 2001;357:1851–3.
[143] Metlay JP, Hofmann J, Cetron MS, et al. Impact of penicillin susceptibility on medical outcomes for adult patients with bacteremic pneumococcal pneumonia. Clin Infect Dis 2000;30:520–8.
[144] Mainous AG III, Hueston WJ, Eberlein C. Colour of respiratory discharge and antibiotic use. Lancet 1997;350:1077.
[145] Mainous AG III, Zoorob RJ, Oler MJ, et al. Patient knowledge of upper respiratory infections: implications for antibiotic expectations and unnecessary utilization. J Fam Pract 1997;45:75–83.
[146] Nyquist AC, Gonzales R, Steiner JF, et al. Antibiotic prescribing for children with colds, upper respiratory tract infections, and bronchitis. JAMA 1998;279:875–7.
[147] Gonzales R, Steiner JF, Maselli J, et al. Impact of reducing antibiotic prescribing for acute bronchitis on patient satisfaction. Eff Clin Pract 2001;4:105–11.
[148] Kleinman A, Eisenberg L, Good B. Culture, illness, and care: clinical lessons from anthropologic and cross-cultural research. Ann Intern Med 1978;88:251–8.
[149] Gonzales R, Wilson A, Crane LA, et al. What’s in a name? Public knowledge, attitudes, and experiences with antibiotic use for acute bronchitis. Am J Med 2000;108:83–5.
[150] Hamm RM, Hicks RJ, Bemben DA. Antibiotics and respiratory infections: are patients more satisfied when expectations are met? J Fam Pract 1996;43:56–62.
[151] Mangione-Smith R, McGlynn EA, Elliott MN, et al. The relationship between perceived parental expectations and pediatrician antimicrobial prescribing behavior. Pediatrics 1999;103:711–8.
[152] Hutchinson JM, Foley RN. Method of physician remuneration and rates of antibiotic prescription. CMAJ 1999;160:1013–7.
[153] Metlay JP, Shea JA, Crossette LB, et al. Tensions in antibiotic prescribing: pitting social concerns against the interests of individual patients. J Gen Intern Med 2002;17:87–94.
[154] Bauchner H, Pelton SI, Klein JO. Parents, physicians, and antibiotic use. Pediatrics 1999;103:395–401.
[155] Gonzales R, Steiner JF, Lum A, et al. Decreasing antibiotic use in ambulatory practice: impact of a multidimensional intervention on the treatment of uncomplicated acute bronchitis in adults. JAMA 1999;281:1512–9.
[156] Hueston WJ, Jenkins R, Mainous AG III. Does drug treatment of patients with acute bronchitis reduce additional care seeking? Evidence from the Practice Partner Research Network. Arch Fam Med 2000;9:997–1001.
[157] Jefferson T, Demicheli V, Deeks J, et al. Neuraminidase inhibitors for preventing and treating influenza in healthy adults. Cochrane Database Syst Rev 2000;CD001265.
[158] Randomised trial of efficacy and safety of inhaled zanamivir in treatment of influenza A and B virus infections. The MIST (Management of Influenza in the Southern Hemisphere Trials) Study Group. Lancet 1998;352:1877–81.
[159] Kaiser L, Briones MS, Hayden FG. Performance of virus isolation and Directigen Flu A to detect influenza A virus in experimental human infection. J Clin Virol 1999;14:191–7.
[160] Noyola DE, Clark B, O’Donnell FT, et al. Comparison of a new neuraminidase detection assay with an enzyme immunoassay, immunofluorescence, and culture for rapid detection of influenza A and B viruses in nasal wash specimens. J Clin Microbiol 2000;38:1161–5.
[161] Jefferson TO, Tyrrell D. Antivirals for the common cold. Cochrane Database Syst Rev 2001;CD001243.
[162] McColl MD, Corser RB, Bremner J, et al. Respiratory syncytial virus infection in adult BMT recipients: effective therapy with short duration nebulised ribavirin. Bone Marrow Transplant 1998;21:423–5.
[163] Hueston WJ. A comparison of albuterol and erythromycin for the treatment of acute bronchitis. J Fam Pract 1991;33:476–80.
[164] Hueston WJ. Albuterol delivered by metered-dose inhaler to treat acute bronchitis. J Fam Pract 1994;39:437–40.

[165] Melbye H, Aasebo U, Straume B. Symptomatic effect of inhaled fenoterol in acute bronchitis: a placebo-controlled double-blind study. Fam Pract 1991;8:216–22.

[166] Littenberg B, Wheeler M, Smith DS. A randomized controlled trial of oral albuterol in acute cough. J Fam Pract 1996;42:49–53.

[167] Smucny JJ, Flynn CA, Becker LA, et al. Are beta2-agonists effective treatment for acute bronchitis or acute cough in patients without underlying pulmonary disease? A systematic review. J Fam Pract 2001;50:945–51.

[168] Douglas RM, Chalker EB, Treacy B. Vitamin C for preventing and treating the common cold. Cochrane Database Syst Rev 2000;CD000980.

[169] Marshall I. Zinc for the common cold. Cochrane Database Syst Rev 2000;CD001364.

[170] Melchart D, Linde K, Fischer P, et al. Echinacea for preventing and treating the common cold. Cochrane Database Syst Rev 2000;CD000530.

[171] Gilroy CM, Steiner JF, Byers T, et al. Echinacea and truth in labeling. Arch Intern Med 2003;163:699–704.

[172] Matthys H, Eisebitt R, Seith B, et al. Efficacy and safety of an extract of Pelargonium sidoides (EPs 7630) in adults with acute bronchitis. A randomised, double-blind, placebo-controlled trial. Phytomedicine 2003;10(Suppl 4):7–17.

[173] Linder JA, Singer DE. Health-related quality of life of adults with upper respiratory tract infections. J Gen Intern Med 2003;18:802–7.