Upper Respiratory Infections and Acute Bronchitis

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1 Introduction

Upper respiratory infections include the following: uncomplicated upper respiratory infections also known as the "common cold," acute otitis media, pharyngitis/tonsillitis, and acute sinusitis. These conditions, along with acute bronchitis, are very common illnesses that are commonly seen in outpatient settings and are widely treated with antibiotics. In fact, these conditions are the primary indications for outpatient antibiotic prescriptions. These conditions tend to have overlapping clinical characteristics yet evidence regarding the utility of antimicrobial treatments varies across conditions.

2 Uncomplicated Upper Respiratory Infection/Common Cold

2.1 Clinical Description

Uncomplicated upper respiratory infections (URIs) are characterized by rhinorrhea, nasal congestion, sneezing, sore or "scratchy" throat, and cough [1]. The incubation period varies between 48 and 72 h. While a low-grade fever in some cases is present, in adults, temperature elevation is rare. Early symptoms may be minimal and limited to malaise and nasal symptoms. The nasal discharge is initially clear and watery. There is a subsequent transition period where the nasal discharge becomes viscous, opaque, and discolored (white, yellow, green) [2]. The color of the secretions is not predictive of a bacterial infection. The clinical presentation is similar in both adults and children. The episode tends to be self-limited. The median duration of a cold is 1 week, with most patients improving by the 10th day; however, lingering symptoms may last up to 2 weeks.

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2.2 Epidemiology

URIs, or the "common cold," are exactly as the name implies – common. URIs are consistently one of the five most common diagnoses in ambulatory physician office visits [3, 4]. Adults have two to four URIs annually, and children in day care have as many as six or seven [5, 6].

The significant costs of URIs can be conceptualized as both direct and indirect costs. The direct costs of URIs include the costs associated with the substantial number of office visits. URIs account for more than 36 million physician office visits a year [7]. In addition, microbiologic and laboratory diagnostic tests are sometimes performed but are of dubious clinical value and, therefore, contribute unnecessarily to the cost of URIs [8]. The total economic impact of non-influenza-related URIs has been estimated to approach $40 billion annually (direct costs, $17 billion per year; and indirect costs, $22.5 billion per year) in the United States [9].

Indirect costs for URIs include productivity losses related to lost workdays for adults who are sick as well as adults who have to deal with sick children. Other indirect costs that are many times overlooked are the impact of URIs on missed opportunities to immunize young children. Although the interpretation of guidelines by the American Academy of Pediatrics and the Advisory Committee on Immunization Practices, particularly for fever and moderate illness, rests with the clinician [10, 11], a large proportion of children are not immunized on schedule due to visits for URIs [12]. This finding also suggests additional visits for immunizations thereby requiring additional direct costs and indirect costs inherent in taking children to the physician's office.

The mechanisms of transmission suggest that URIs can be spread through contact with inanimate surfaces [13] and hand-to-hand contact [14]. URIs have a seasonal variation with an increased prevalence in the United States between September and March. It is unclear why this variation exists, although it may be related to increased crowding of indoor populations in the colder months. Temperature is not the key to seasonal variation without the presence of a pathogen. Evidence from Antarctica showed that spacious well-ventilated rooms reduced transmission of URIs as compared to crowded poorly ventilated rooms regardless of temperature [15].

2.3 Etiology

Viruses have been shown to be the major pathogens in URIs [16]. One study established viral etiology in 69% of URIs [17]. Rhinoviruses were found in 52% of the patients by viral culture or PCR assay. *Coronaviruses* were the second most common group of causative agents, followed by *influenza A or B virus*. Identified bacterial pathogens were *Chlamydia pneumoniae*, *Haemophilus influenzae*, *Streptococcus pneumoniae*, and *Mycoplasma pneumoniae*. None of the patients had beta-hemolytic group A *Streptococcus*. In terms of bacterial pathogens, infections without evidence of a viral infection occurred in only 0.05% of the cases.

2.4 Treatment

A variety of studies in the 1990s showed a high rate of prescribing antibiotics for URIs [18, 19]. More recent data have indicated a drop in the prescribing of antibiotics; however, the use of antibiotics is still far from optimal [20]. Controlled trials of antimicrobial treatment of URIs have consistently demonstrated no benefit [21, 22]. In eight trials of antimicrobial treatment of URIs, six found no difference between the groups either in terms of improvement or in terms of complications. Complications tend to be minimal and occur at a rate of 10–15%. One trial found some slight benefit in decreasing the presence of purulent rhinitis [23]. Another found a decrease in rhinorrhea at day 5 but no difference between the groups at day 10 [24]. Similarly, an additional trial attempted to isolate "bacterial colds" for which antibiotics might be effective treatments [25]. Although there was some indication of patient improvement at day 5, the differences were gone by day 10. It is important to remember that the normal presentation of a URI is a week to 10 days.

Few successful treatments have been identified. Vitamin C, zinc gluconate, and Echinacea have all shown mixed results [26, 27]. Antihistamines, with a few exceptions, have not been shown to be effective treatments [28]. The most effective symptomatic treatments are over-the-counter decongestants [9].

3 Acute Sinusitis

3.1 Clinical Description

Acute sinusitis has considerable overlap with URIs in its constellation of signs and symptoms. One half to two thirds of patients with sinus symptoms seen in primary care are unlikely to have sinusitis [29]. In 300 patients who presented with a URI, 19% had radiographic evidence of maxillary sinusitis but had no symptoms of sinus infection [25]. URIs are often precursors of sinusitis, and, at some point, symptoms from each condition may overlap. Sinus inflammation from a URI, without bacterial infection, is also common. In a series of 60 children undergoing computerized tomography (CT) for non-sinus-related diagnoses, 47% had evidence sinus inflammation with no clinical signs of sinusitis and with complete resolution following their viral illness [30].

Acute sinusitis tends to start with a URI that leads to sinus ostial obstruction. The signs and symptoms that increase the likelihood that the patient has acute sinusitis are a "double sickening" phenomenon whereby the patient seems to improve following the URI and then deteriorates, exhibiting symptoms such as maxillary toothache, purulent nasal discharge, poor response to decongestants, and a history of discolored nasal discharge [31, 32]. Other authors have stressed that the symptoms need to persist longer than 1 week to distinguish sinusitis from a URI [33]. It should be pointed out that the commonly used sign of facial pain or swelling has low sensitivity for acute sinusitis [32].

3.2 Epidemiology

Since sinusitis is most often a complication of upper respiratory viral infections, it follows the same seasonal pattern as colds. This pattern produces a winter peak with more cases seen than those exposed to upper respiratory tract infections.

In children seen in a large health system, sinusitis is frequently found as a comorbidity with otitis media. Nearly half of all children with sinusitis also had otitis media [34]. Children are also more likely to have posterior ethmoidal and sphenoid inflammation, while adults have mainly maxillary and anterior ethmoidal sinusitis [35]. Some medical conditions may increase the risk for sinusitis; these include cystic fibrosis, asthma, immunosuppression, and allergic rhinitis [36]. Cigarette smoking may also increase the risk of bacterial sinusitis during a cold because of reduced mucociliary clearance.

3.3 Etiology

Sinus inflammation can be caused by viral, fungal, and bacterial infections as well as allergies. The majority of acute sinusitis is caused by viral infection. As indicated above, many cases of the common cold have concomitant sinus inflammation. The inflammation associated with viral infections clears without additional therapy.

Bacterial superinfection of URIs is rare and occurs in only 0.5–1% of colds. Studies examining the treatment of sinusitis confirm that response rates to antibiotics are either small [37]. When sinusitis is confirmed by a CT scan, response rates to antibiotics are improved [38].

Cultures of material obtained from patients with sinusitis show that the most prevalent organisms are *Strep. pneumoniae* and, especially in smokers, *H. influenzae.* These two organisms are present in 70% of cases of bacterial acute sinusitis [39]. When antibiotics are used for the treatment of bacterial sinusitis, the selection of antibiotics should include sufficient coverage of these two organisms.

Fungal sinusitis are very rare and usually occur in immunosuppressed individuals or those with diabetes mellitus [39].

3.4 Treatment

Antibiotics are commonly prescribed for adult patients who present with complaints that are consistent with acute sinusitis. The effectiveness of antibiotics is unclear. Three recent placebo-controlled, double-blind, randomized trials in general practice settings have yielded mixed results [37, 38, 40]. Two of these trials showed no beneficial effect of antibiotics [37, 40]; the third trial, however, demonstrated a significant effect of penicillin and amoxicillin [38]. The trial showing an effect used more stringent enrollment criteria than the other two; the criteria in the trial are more consistent with those used in daily practice by primary care physicians. These data suggest that patients with more severe signs and symptoms may benefit from an antibiotic. If an

antibiotic is to be used, some evidence with trimethoprim/sulfamethoxazole suggests that short-duration treatment (e.g., 3 days) is as effective as longer treatment [41]. Further, narrow-spectrum agents seem as effective as broad-spectrum agents [42].

In patients with severe signs and symptoms, antibiotics have some utility in treating acute sinusitis. If antibiotics are to be used, then short-course therapy with narrow-spectrum agents is recommended. The key to the judicious use of antibiotics is to first make an accurate diagnosis of sinusitis rather than overtreating URIs.

4 Acute Otitis Media

4.1 Clinical Description

The evaluation and management of otitis media has been subject to a wide variance in approaches. The variation in management of otitis media is typified in an examination of the management of otitis media in nine countries in the mid-1980s [43]. In this study, antibiotics were used over a wide range (31–98%) of episodes of otitis media with similar variation in the types of antibiotics used and duration of therapy. To help bring some consensus to the process, the American Academy of Pediatrics issued a guideline for the evaluation and treatment of otitis media in 2004 [44]. While the guideline suffers from a lack of definitive evidence in several areas of care, the recommendations are an effective tool for bringing some clarity to an issue that has suffered from a wide variation in management strategies.

The AAP guideline recommends that the diagnosis of otitis media requires three essential components: an acute onset of illness, presence of a middle ear effusion, and signs and symptoms of middle ear inflammation. Middle ear effusion is evident in children with bulging of the tympanic membrane, reduced or absent mobility of the membrane with pneumatic otoscopy, an air–fluid level behind the membrane, and pain in the effected side. Inflammatory signs noted in the report include erythema of the tympanic membrane along with pain on that side. In considering all these factors, the combination of reduced mobility, erythema, and a bulging tympanic membrane is the best predictor of otitis media.

The most essential step in managing otitis media is assuring that the diagnosis is correct. Otitis media may be overdiagnosed, especially in younger children, which complicates the evaluation of treatment effectiveness. Studies show that a physician's certainty about the diagnosis of otitis media is dependent on the patient's age. In a multinational study, it was found that physicians were certain of the diagnosis in only 58% of children under the age of 1 [43]. This increased to 66% in those between 1 year and 30 months of age and up to 73% in those over 30 months of age.

4.2 Epidemiology

Historically, acute otitis media has been one of the most common pediatric conditions seen in primary care. However, since the introduction of vaccines

against common respiratory pathogens, there is evidence that the frequency of this problem has decreased considerably. In the Netherlands, visits to general practitioners for otitis media with effusion in children under the age of 2 fell by 66% between 1995 and 2003 [45]. A similar decrease in visits for acute otitis in children has been reported in a large health system in the United States [46], with a smaller reduction in visits noted in the emergency department setting [47]. The introduction of *H. influenzae B* vaccine in the 1980s, followed by universal childhood immunization with conjugated *Strep. pneumoniae,* may be responsible for the reduction in otitis media cases encountered.

Since otitis media is a complication of an upper respiratory infection, it has a peak incidence in the winter when colds are most likely to occur. Unlike sinusitis, which is more likely to affect adults, otitis media is predominantly a disease of younger children with a peak incidence between 6 and 36 months of age [48]. Otitis media occurs with varying frequency in children. In a large population study, it was found that during the first 3 years of life about a third of children never had otitis media and another third had one or two episodes, while the remaining third had three or more episodes.

Otitis media occurs more often in males, children in lower socioeconomic groups, and in certain ethnic groups such as native Americans. Because of differences in the mechanics of the posterior pharynx and Eustachian tube, children born with craniofacial congenital abnormalities such as cleft lip/palate and those with Trisomy 21 also are more likely to have otitis media as a complication of a cold.

4.3 Etiology

Otitis media arises from Eustachian tube dysfunction that accompanies URIs or allergic rhinitis. Inflammation of the Eustachian tube and middle ear results in tube occlusion and fluid accumulation in the middle ear space. Eustachian tube obstruction is more common in younger children because of less cartilage support of the tube making collapse more likely. The Eustachian tube obstruction not only causes entrapment of existing fluid but also produces a negative pressure in the middle ear that results in additional fluid accumulation that characterizes serous otitis media. Contamination of this fluid with bacteria results in acute suppurative otitis media.

Suppurative otitis media is most often caused by the same organisms that result in sinusitis. Studies of middle ear aspirates suggest that *Strep. pneumonia* is the most common bacterial cause of otitis media and is found in about 40% of effusions. *H. influenzae* accounts for approximately another 20%. *B. catarrhalis* and *Staphylococcus aureus* each make up fewer than 10% of cases. In neonates, gram-negative species also should be considered as potential etiologic agents.

Otitis media also may result from noninfectious obstruction of the Eustachian tube. Allergic rhinitis, as noted above, is one such mechanism. Other causes include enlargement of the adenoids and posterior pharyngeal tumors.

4.4 Treatment

Treatment recommendations from the AAP/AAFP guidelines for the management of acute otitis media suggest that observation rather the initial use of antibiotics is appropriate depending on the child's overall health, age, severity of illness, and likelihood that they can follow-up if necessary. For healthy children over the age of 2, antibiotics are recommended only if the child is severely ill; if the child is mildly ill or if the diagnosis is uncertain, then observation is acceptable. For children younger than this, antibiotics are recommended for a certain diagnosis of otitis media and for those under age 6 months where the diagnosis is uncertain. Antibiotics are not recommended for use in healthy children between 6 months and 2 years who have an uncertain diagnosis (AAP Subcommittee). If patients who are observed fail to improve in 48–72 h, then antibiotic therapy is recommended.

Based on the AAP/AAFP guidelines, routine observation or "wait and see protocol (WASP)" as an alternative to universal antibiotic use has been evaluated in emergency room setting. A randomized trial of the WASP approach compared with routine antibiotics showed that antibiotic use was reduced from 62 to 13% with no differences in prolonged fever, ear pain, or unscheduled subsequent visit for the ear infection [49]. Despite evidence that the WASP or observation period is effective, primary care physicians have been slow to adopt this in practice [50].

When antibiotics are selected for the management of acute suppurative otitis media, selection of an agent should provide coverage for the two most common organisms, the AAP/AAFP recommends initial treatment with amoxicillin at a dose of 80–90 mg/kg per day. Second, the duration of antibiotic treatment is unclear. In a meta-analysis of trials that compared short-duration antibiotic therapy with the traditional 10 day course, no benefit was found of using longer courses of treatment; however, methodologic problems may complicate the interpretation of these results [51]. In their guidelines, the AAP/AAFP recommends that a 5–7 day course of antibiotics should be sufficient for treatment.

In addition to short-course therapy, a single intramuscular dose therapy of ceftriaxone has been shown to be equally beneficial to longer courses of amoxicillin [52], cefaclor [53], or trimethoprim–sulfamethoxazole [54] for the treatment of acute suppurative otitis media. Where antibiotic resistance to *S. pneumonia* is high or where patient compliance is an issue, ceftriaxone may be a viable alternative. In addition, some studies have evaluated the use of a single dose of azithromycin (30 mg/kg) for treatment of uncomplicated otitis media. In a review of these studies, the overall success rate was 82% [55]. Macrolide resistance to *S. pneumoniae* was the largest impediment to success. Based on this, it was suggested that

single-dose azithromycin may be an alternative in areas with resistance to *S. pneumoniae* is uncommon.

The primary concern in the treatment of otitis media is a primary treatment failure (i.e., persistent illness or an early recurrence of disease following initial therapy of a new otitis episode) [56]. A meta-analysis of 33 randomized trials supports initial antibiotic use demonstrated no significant differences in failure rates when comparing "standard" or first-line (penicillin, amox/ampicillin, erythromycin, and sulfamethoxazole) and "extended-spectrum" or second-line antibiotics or with duration of therapy. The only factor that appears to be consistently linked to a higher likelihood of a primary treatment failure is a child's age [57, 58], with children younger than 2 years of age having treatment failures in 26–37.5% of cases. For older children, treatment failures occur in 2–19% of episodes [57, 58].

Also of concern is how to manage a new case of otitis media when a previous treatment failure has occurred. In a study that examined failure rates in new infections for children who had a previous treatment failure, there was no benefit of starting therapy with an extended-spectrum agent compared to "first-line" drugs. Thus it appears that in a case of previous treatment failure, new cases should be managed with narrow-spectrum agents such as amoxicillin or TMP–SMX [59].

The use of second-line antibiotics when a first-line agent will suffice creates two problems. First, in most cases the use of broad-spectrum drugs adds significant expense to therapy. Others have reported that use of second-line agents compared to amoxicillin or SMX–TMP adds 16% to the overall cost of the episode [56]. Since the results of this study show comparable failure rates for first- and second-line antibiotics, there appears to be no justification for this additional cost.

Second, the injudicious use of broad-spectrum antibiotics may increase the potential for future development of antibiotic resistance. The overuse of antibiotics has been proposed as one reason for the observed growth in antibiotic resistance reported in common childhood organisms such as *S. pneumoniae*. Otitis media is a condition in which antibiotics are frequently prescribed for children and where broad-spectrum antibiotics may be used unnecessarily. Limiting the use of broad-spectrum drugs to situations in which they are beneficial (i.e., managing the resistant case of otitis) may help reduce further development of drug resistance in children.

5 Tonsillitis/Pharyngitis

5.1 Clinical Description

Sore throat is a common reason that patients consult with a physician. Most of these are viral infections related to upper respiratory infections, but about 15–30% are secondary to infection with group A beta-hemolytic streptococcus. The primary role of the physician is to differentiate streptococcal pharyngitis from viral illnesses.

Since most patients with sore throats probably do not visit their doctor, it is difficult to state with any certainty how often sore throats occur in healthy populations. However, pharyngitis is one of the most common diagnoses for physician office

visits. Estimates from 2005 suggest that more than 11 million visits in the United States each year are for pharyngitis [7]. Frequently antibiotics are prescribed for these conditions without evidence of a bacterial etiology.

5.2 Epidemiology

Both viral and group A streptococcal pharyngitis have peak occurrences in the winter and early spring. Streptococcal infection, in particular, can be recognized in epidemic patterns frequently affecting groups that spend considerable time together in close quarters such as day cares, schools, and places of employment. Strep throat also is related to patient age. While infection in the very young (< 1 year old) is uncommon, the peak occurrence for strep throat is between 5 and 15 years of age with diminished risk over the age of 20.

5.3 Etiology

The most common causes of pharyngitis are respiratory viruses. Adenovirus and the rhinoviruses account for about 80% of cases of sore throat in children that are seen by physician [60, 61]. Coxackievirus, herpesvirus, and Epstein–Barr virus can cause tonsillitis but are less common that adenovirus [62]. Adenovirus, coxackievirus, and Epstein–Barr virus can cause exudative pharyngitis that can mimic the appearance of streptococcal infection. While exudative tonsillitis is thought to be a hallmark of group A streptococcal infection, this sign is actually present more often from adenovirus than streptococcus. It is important to identify group A streptococcal infections because trials of antibiotics in undifferentiated sore throat populations show little benefit [63].

Group A beta-hemolytic streptococcus can cause an acute tonsillopharyngitis and may colonize the oropharynx without symptoms. The asymptomatic carrier rate of group A strep ranges from about 10 to 30% of healthy children, a rate that nearly matches the true infection rate [64, 65]. This means that in testing for group A streptococcus, positive tests are just as likely to occur from carriers of group A strep who have a concomitant virus as those actually infected with the organism. In contract to group A streptococcal tonsillopharyngitis, treatment of the carrier state is not necessary and does not reduce symptoms or reduce complications [66].

The reasons for antibiotic treatment of beta-hemolytic group A streptococcal pharyngitis are to alleviate symptoms, reduce the spread of disease, and reduce the risk of suppurative and nonsuppurative complications. Although some authors have suggested that antibiotics are not justified to reduce the risk of rheumatic fever, a complication of beta-hemolytic group A streptococcal pharyngitis, the American Heart Association in 2009 still recommends antibiotic treatment [67, 68].

Differentiating group A streptococcal pharyngitis from viral disease is the most vexing problem in the management of acute sore throat. The clinical impression of the treating physician has been shown to be fairly inaccurate at making this

differentiation [69–71]. A clinical prediction rule for presence of strep throat that has some utility uses the presence of tonsillar exudate, pharyngeal exudate, or exposure to strep throat infection and the absence of tender anterior cervical nodes, tonsillar enlargement, or exudate. No individual element of history-taking or physical examination is accurate enough by itself to rule in or rule out strep throat [72]. Another dilemma in identifying group A strep in patients with pharyngitis is the sensitivity of rapid group A antibody kits compared to a throat culture. Many studies have shown that a rapid test is less sensitive than the culture for identifying the presence of group A strep. The rapid tests have a high degree of specificity, but their sensitivity in clinical practice can be unacceptably low. Sensitivities for the rapid test compared to a standard blood agar culture vary considerably but are generally in the range of 60–70%. Studies also have demonstrated that in circumstances when the colony counts are low, rapid tests are more likely to miss the presence of group A streptococcus. However, when the seroconversion of ASO titers is used as the gold standard for infection, rapid tests perform very well [69]. It is likely that rapid tests miss patients who have a small number of organisms and who are likely to be colonized instead of infected. Thus, rapid testing may be more specific in identifying patients with actual strep-related disease than cultures, which also identify those who are likely to be carriers. This comparison suggests that follow-up throat cultures are not necessary and may actually confuse treatment decisions. Rapid strep testing without culture also has been shown to be the most cost-effective approach to managing acute pharyngitis [73].

As indicated above, reports regarding the role of Chlamydia and Mycoplasma indicate that these two organisms also may be associated with acute pharyngitis. However, there have been few treatment trials that demonstrate any benefit of treating non-group A streptococcus with antibiotics that would treat either of these organisms. In a study using erythromycin to treat non-group A strep pharyngitis [74], patients who received placebo had the same speed of symptom resolution as those treated with active antibiotics.

5.4 Treatment

5.4.1 Group A Beta-Hemolytic Streptococcal Tonsillopharyngitis

Once group A streptococcus has been implicated in the infection, the choice of antibiotic is controversial. With only scant evidence that treatment reduces the symptomatic period and a low risk of complications from untreated group A streptococcal pharyngitis, some investigators suggest that antibiotic treatment carries more risks than not treating and encourages future health seeking and antibiotic expectations for future sore throats [75]. However, formal decision analyses suggest that in cases of moderate probability of strep throat (40–85%) with symptom duration of 2 days or less, rapid strep testing and treatment is beneficial [76].

Selection of an appropriate antibiotic and duration of therapy are important considerations in treating strep pharyngitis. Penicillin V resistance in group A strep

as well as erythromycin resistance has led to investigations of other drugs for management of strep throat. Since streptococcal pharyngitis is a self-limited problem even without antibiotic therapy, much of this resistance has been based on positive throat cultures following the termination of treatment. This may be misleading since colonized patients may continue to harbor streptococcus even after therapy.

When drug failure rates are examined with penicillin, cultures remain positive in 11–45% of treated patients [77, 78]. However, single-dose therapy with amoxicillin at 40 mg/kg/day for 10 days appears to be very successful resulting in excellent clinical responses and low rates (5–10%) of posttreatment carrier rates [77, 78]. Treatment with other agents such as azithromycin and clarithromycin produces no better results than amoxicillin or penicillin V [79–81]; however, these treatments amount to a much greater expense.

Attempts at "short-course" therapy have been studied with azithromycin [82]. Both short-course treatment with azithromycin and 10 days of cefaclor have exactly the same clinical cure rates (86%) by day 3 of therapy. However, patients treated with cefaclor were less likely to become recolonized with group A strep over the next 45 days than those treated with the short course of azithromycin (20% vs. 55%). Since the significance of rapid recolonization is still unclear, short-course therapy with azithromycin or other antibiotics still requires additional investigation.

5.4.2 Group A Streptococcal Carriers

While the carrier rate does not require treatment [66], some clinicians attempt to eradicate those colonized by group A strep to prevent spread to other family members and close contacts. A regimen of intramuscular penicillin V plus oral rifampin has been shown to reverse the carrier status in 93% of patients treated [83]. There have been no studies performed more recently that have explored whether this regimen remains effective with increased group A strep resistance to penicillin.

5.4.3 Non-group A Streptococcal Pharyngitis

Despite evidence that Chlamydia and Mycoplasma may be associated with acute pharyngitis, there have been no studies that have shown a benefit from treatment of patients with non-group A streptococcal pharyngitis with antibiotics: studies with penicillin [69], which would not be expected to cover these agents, and macrolides [74], which would have not shown any significant improvement over placebo. Until specific tests that can rapidly identify these organisms are developed which would allow for targeted treatment and studies can demonstrate that treatment reduces symptoms and complications, indiscriminate antibiotic therapy for non-group A strep pharyngitis should be avoided.

6 Acute Bronchitis

6.1 Clinical Description

Acute bronchitis is an inflammatory condition of the tracheobronchial tree usually associated with a generalized respiratory infection. Cough begins early in the course of the illness and is the most prominent feature of the condition. An initially dry cough may later result in sputum production which characteristically changes from clear to discolored in the later stages of the illness. The cough may last for a significant time. Although the duration of the condition is variable, one study showed that 50% of patients had a cough for more than 3 weeks and 25% had a cough for more than 4 weeks [84].

Patients with acute bronchitis usually have a viral respiratory infection with transient inflammatory changes that produce sputum and symptoms of airway obstruction. Acute bronchitis is essentially a diagnosis of exclusion. The history should include information on cigarette use, exposure to environmental toxins, as well as medication history (e.g., use of angiotensin-converting enzyme inhibitors). The chronicity of the cough should be established to distinguish acute bronchitis from chronic bronchitis since they have different treatments.

Both acute bronchitis and pneumonia can present with fever, constitutional symptoms, and a productive cough. While patients with pneumonia often have rales, this finding is neither sensitive nor specific for the illness. When pneumonia is suspected on the basis of a presence of a high fever, constitutional symptoms, severe dyspnea, and certain physical findings or risk factors, a chest radiograph should be obtained to confirm the diagnosis.

Asthma and allergic bronchospastic disorders can mimic the productive cough of acute bronchitis. When obstructive symptoms are not obvious, mild asthma may be diagnosed as acute bronchitis. Further, since respiratory infections can trigger bronchospasm in asthma, patients with asthma that occurs only in the presence of respiratory infections resemble patients with acute bronchitis.

Asthma should be considered in patients with repetitive episodes of acute bronchitis. Patients who repeatedly present with cough and wheezing can be given full spirometric testing with bronchodilation or provocative testing with a methacholine challenge test to help differentiate asthma from recurrent bronchitis.

Finally, nonpulmonary causes of cough should enter the differential diagnosis. In older patients, congestive heart failure may cause cough, shortness of breath, and wheezing. Reflux esophagitis with chronic aspiration can cause bronchial inflammation with cough and wheezing. Bronchogenic tumors may produce a cough and obstructive symptoms.

6.2 Epidemiology

Acute bronchitis in the otherwise healthy adult is one of the most common medical problems encountered in primary care [4, 7]. The prevalence of acute bronchitis peaks in the winter and is much less common in the summer.

6.3 Etiology

Viral infection is considered the primary cause of most episodes of acute bronchitis. A wide variety of viruses have been shown as causes of acute bronchitis including influenza, rhinovirus, adenovirus, coronavirus, parainfluenza, and respiratory syncytial virus [85]. Nonviral pathogens including *Mycoplasma pneumoniae* and *C. pneumoniae* (TWAR) have also been identified as causes [86, 87].

The etiologic role of bacteria like *H. influenzae* and *S. pneumoniae* in acute bronchitis is unclear since these bacteria are common upper respiratory tract flora. Sputum cultures for acute bronchitis are therefore difficult to evaluate since it is unclear whether the sputum has been contaminated by pathogens in the nasopharynx.

6.4 Evaluation

Usually, laboratory and imaging tests are not needed in the diagnosis of acute bronchitis. However, a new test under consideration might be helpful in differentiating viral acute bronchitis from more serious bacterial infections such as pneumonia. By measuring procalcitonin, a precursor to the hormone calcitonin, Christ-Crain and colleagues have been able to distinguish patients at high risk for bacterial infections (those with higher procalcitonin levels) from those with low risk for bacterial infection. Evaluation of this method in the emergency department has led to reductions in antibiotic prescribing without any differences in clinical outcomes for patients presenting with acute cough syndromes [88]. While a point-of-care version of the test for procalcitonin has been developed that can be done quickly in a physician's office, the test is still expensive and has not been evaluated outside the emergency department.

6.5 Treatment

Antibiotic treatment for acute bronchitis is quite common with evidence indicating that 60–75% of adults visiting a doctor for acute bronchitis receiving an antibiotic [19, 89]. Clinical trials of the effectiveness of antibiotics in treating acute bronchitis have had mixed results. One reason for the lack of consensus is that in each of the nine trials, different antibiotics were used as well as different outcomes. In an effort to quantitatively review the data, two different meta-analyses were recently conducted [90, 91]. In the Fahey et al., meta-analysis resolution of cough was not affected by antibiotic treatment and neither was clinical improvement at re-examination. Importantly, the side-effects of antibiotics were more common in the antibiotic groups compared to placebo. The Smucny et al., meta-analysis concluded that antibiotics may be modestly effective for a minority of patients with acute bronchitis, although it is unclear which subgroups might benefit. The conclusion of both meta-analyses was that the benefits or antibiotics are marginal and are not useful for the general group of patients with acute bronchitis.

Recent data from clinical trials suggest that bronchodilators may provide effective symptomatic relief to patients with acute bronchitis [92, 93]. Treatment with bronchodilators demonstrated significant relief of symptoms including faster resolution of cough, as well as return to work. One study evaluated the effect of albuterol in a population of patients with undifferentiated cough and found no beneficial effect [94]. Since a variety of conditions present with cough, there may have been some misclassification in generalizing this to acute bronchitis.

Key Points

- Upper respiratory infections and acute bronchitis are common illnesses that are account for a large proportion of total outpatient healthcare utilization as well as nearly 75% of prescribed outpatient antibiotics.
- Evidence does not support the use of antibiotics for the common cold, acute bronchitis, initial cases of otitis media with effusion, and non-group A streptococcal pharyngitis. These conditions are self-limited and currently are optimally treated with symptomatic medicines.
- Although the data are mixed regarding the utility of antibiotic treatment for acute sinusitis, otitis media, and group A streptococcal pharyngitis, antibiotics may have some benefit. Short-course therapy with narrow-spectrum antibiotics appropriate for the likely pathogen is recommended.

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