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# Epidemiology of Community-Acquired Respiratory Tract Infections in Adults

## Incidence, Etiology, and Impact

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Upper respiratory tract infections are the most common types of infectious diseases among adults. It is estimated that each adult in the United States experiences two to four respiratory infections annually. The morbidity of these infections is measured by an estimated 75 million physician visits per year, almost 150 million days lost from work, and more than \$10 billion in costs for medical care. Serotypes of the rhinoviruses account for 20 to 30 percent of episodes of the common cold. However, the specific causes of most upper respiratory infections are undefined. Pneumonia remains an important cause of morbidity and mortality for nonhospitalized adults despite the widespread use of effective antimicrobial agents. There are no accurate figures on the number of episodes of pneumonia that occur each year in ambulatory patients. In younger adults, the atypical pneumonia syndrome is the most common clinical presentation; *Mycoplasma pneumoniae* is the most frequently identified causative agent. Other less common agents include *Legionella pneumophila*, influenza viruses, adenoviruses, and *Chlamydia*. More than half a million adults are hospitalized each year with pneumonia. Persons older than 65 years of age have the highest rate of pneumonia admissions, 11.5 per 1,000 population. Pneumonia ranks as the sixth leading cause of death in the United States. The pathogens responsible for community-acquired pneumonias are changing. Forty years ago, *Streptococcus pneumoniae* accounted for the majority of infections. Today, a broad array of community-acquired pathogens have been implicated as etiologic agents including *Legionella* species, gram-negative bacilli, *Hemophilus influenzae*, *Staphylococcus aureus* and nonbacterial pathogens. Given the diversity of pathogenic agents, it has become imperative for clinicians to establish a specific etiologic diagnosis before initiating therapy or to consider the diagnostic possibilities and treat with antimicrobial agents that are effective against the most likely pathogens.

Infections of the respiratory tract are the most common types of infectious diseases in the United States. A National Health Survey conducted in 1981 estimated that well over 200 million episodes of respiratory infection occur each year [1]. Other studies of smaller, more closely monitored populations suggest that the actual number may be two to four times that estimate [2,3]. The range of pathogens responsible for upper and lower respiratory tract infections is myriad and ever-expanding. The morbidity of these infections is staggering in terms of days of disability, lost school or work days and medical costs. Even today, pneumonia continues to be

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"the old man's friend" and is still ranked as the sixth leading cause of death in the United States. This article will review the incidence, significance, etiology, epidemiology, and therapy for the most common types of respiratory infections—the common cold and pneumonia in nonhospitalized patients.

### UPPER RESPIRATORY INFECTIONS

Accurate information regarding the incidence and causes of upper respiratory tract infections among adults in the United States is difficult to find. The majority of patients with minor colds never seek medical assistance. When medical assistance is sought, diagnoses are rarely confirmed by specific laboratory testing. There are no formal surveillance networks to estimate accurately the true number of cases that occur each year. Perhaps the most representative estimates of incidence of upper respiratory infection are contained in the National Health Interview Surveys that are conducted annually by the National Center for Health Statistics. In these surveys, samples of 30,000 to 50,000 households are selected to complete an extensive questionnaire that reviews recent health status. Health statistics are tabulated for more than 100,000 persons who reside in the sample households. The 1980 survey revealed that upper respiratory infections were by far the most common reason questionnaire respondents sought medical advice [4]. This survey estimated that more than 75 million visits to physician offices, emergency rooms, or outpatient clinics were prompted by upper respiratory infections; influenza-like illnesses accounted for 45 million encounters and common colds, for 30 million. The total number of visits for all other infections, including unspecified viral infections, was 41 million.

A more detailed survey in 1981 estimated the incidence and morbidity of respiratory infections that occurred retrospectively within the previous 12-month period, whether or not a physician had been consulted [1]. From this survey, it was calculated that there are approximately 112 million episodes of influenza-like illness annually in the United States, for an attack rate of 49.7 episodes per 100 persons per year (Table I). The common cold ranked second in frequency with 93 million episodes and an attack rate of 41.4 per 100 persons per year. The morbidity associated with these infections was staggering. Influenza-like illnesses alone accounted for more than 400 million days of restricted activities, or approximately 1.9 days per person per year (Table II). Common colds were responsible for another 250 million days of restricted activity, or 1.2 days per person per year. It was estimated that almost 150 million days were lost from work in 1981 because of upper respiratory conditions, for a rate of 1.4 lost work days per person.

Currently, at least half a dozen viral agents are thought to be responsible for the majority of upper respiratory infections (Table III). However 30 to 40 percent of respiratory infections go undiagnosed even when extensive labo-

**TABLE I** Episodes of Upper Respiratory Infection in Ambulatory Patients

Condition	Episodes (millions)	Episodes per 100 Persons per Year
Influenza	111.8	49.7
Common cold	93.1	41.4
Pneumonia	3.3	1.5
Bronchitis	6.4	2.8

Data from [1].

ratory testing is performed to uncover possible infectious agents. These infections are thought to be caused by as yet unidentified viruses or Chlamydia. Of the known viral agents, rhinoviruses have been implicated as causes of 25 to 30 percent of common cold episodes. More than 110 antigenic serotypes of rhinoviruses have been identified. Because there is no cross-immunity among serotypes, reinfections with antigenically different rhinoviruses are common. Three antigenic serotypes of coronaviruses account for an estimated 5 to 10 percent of illnesses. Influenza viruses, respiratory syncytial virus, adenovirus, and parainfluenza viruses are responsible for another 10 to 15 percent of cases. Occasionally, bacteria such as group A beta-hemolytic streptococci or Mycoplasma such as *M. pneumoniae* cause cold-like syndromes. A recent report has suggested that *M. pneumoniae* and chlamydial organisms are more common causes of pharyngitis than had previously been appreciated, with serologic evidence of Mycoplasma infection in 10.6 percent and Chlamydia in 20.5 percent of patients [5].

Clinically, symptoms of the common cold are generally self-limited and resolve completely with no sequelae. However, occasionally the acute viral infection becomes complicated by secondary otitis media or sinus infection. Primary upper respiratory infections may also cause local changes in the trachea and predispose patients to subsequent bacterial tracheobronchitis or pneumonia.

**TABLE II** Morbidity Associated with Upper Respiratory Infection in Ambulatory Patients

Condition	Days of Restricted Activity* (millions)	Rate per Person per Year
Influenza	428.3	1.9
Common cold	261.8	1.2
Pneumonia	53.5	0.2
Bronchitis	38.7	0.2

\*A total of 141.3 million days lost from work in 1981 for upper respiratory conditions (140.8 days per 100 employed persons per year). Data from [1].

**TABLE III** Agents Associated with the Common Cold

Agent	Antigenic Types	Percent of Cases
Rhinovirus	>110	25–30
Coronavirus	>3	≥10
Influenza virus	3	10–15
Respiratory syncytial virus	1	
Adenovirus	33	
Parainfluenza virus	4	
Other viruses		5–10
Presumed viruses or Chlamydia		30–40
Group A streptococci		5–10
Mycoplasma		5–10

The manner in which the common cold viruses are transmitted from person to person is not well understood. There is reasonable evidence to suggest that exposure to dampness or cold does not in itself precipitate infection. The exact mode of spread may be slightly different for each viral agent. For the influenza and Coxsackie viruses, aerosolization of virus-laden respiratory secretions by coughing or sneezing is thought to be an important route of virus transmission [6]. Infectious droplet nuclei may also be generated by these events. For rhinoviruses, airborne transmission is thought to be less important than direct contact with virus on contaminated hands or other skin surfaces [7]. Transmission is accomplished when viruses are inoculated onto the mucous membranes of the nose or eyes. Transmission of rhinovirus has also been demonstrated in experimental circumstances from hand contact with tabletop surfaces that were contaminated hours before. In either case, spread of common cold viruses occurs readily in settings in which there is close physical contact, such as households, schools, work places, nursing homes, or hospitals. The propensity for case clustering or epidemic spread is great.

Each year in the United States, more than \$10 billion are spent on treatments for the common cold [8]. As yet, no effective antiviral therapy is available for any of the common cold viruses with the exception of influenza A. For influenza A, amantadine hydrochloride has been shown to be effective in modifying the clinical syndrome if it is given early enough in the acute disease stage. Without the availability of specific antimicrobial therapy, treatment for most upper respiratory infections is supportive for symptomatic relief. Antipyretic and analgesic drugs are prescribed for relief of fever, headache, myalgia, and arthralgia. Decongestants and antihistamines are used to relieve nasal stuffiness; antitussives and lozenges are prescribed to reduce the irritation of cough and sore throat. None of these therapies has any effect on the natural history of the acute viral illness.

## PNEUMONIA IN AMBULATORY PATIENTS

Few data exist regarding the incidence, specific causes, or impact of pneumonia in ambulatory adult patients. In the National Health Interview Survey of 1981, it was estimated that 3.3 million cases of pneumonia occurred in ambulatory children and adults, for a rate of 1.5 episodes per 100 persons per year [1]. These estimates are similar to observations made in the Washington Group Health Cooperative Study from 1963 to 1975 in which the adjusted annual rate of pneumonia in adults was 1.2 cases per 100 population per year [3]. In the Washington survey, the highest rates of pneumonia were observed in school-aged children; approximately 15 percent of pneumonias in both children and adults were due to *M. pneumoniae*, on the basis of throat cultures or serologic results.

The crude estimates of pneumonia incidence in ambulatory patients probably grossly under-represent their actual occurrence. Many episodes of pneumonia go unrecognized. In children or adults without compromising underlying diseases, the clinical syndrome is relatively benign, the disease is self-limited, and the symptoms are nonspecific. Although virtually all infected persons have cough, fever, and general malaise, most do not seek medical help. Furthermore, even when pneumonia is present, the extent of infection may not be revealed by findings on the physical examination; the pneumonia may only be identified by radiographic examination of the lungs. Even when the diagnosis of pneumonia is confirmed by chest radiography, an etiologic agent is seldom identified outside of prospective clinical studies. Examination of sputum by stains or cultures is rarely performed because most patients have nonproductive coughs. Serologic studies to document antibody titer increases are carried out infrequently because they are not immediately helpful in establishing the diagnosis in an acutely ill patient and they are expensive. Finally, a specific diagnosis is rarely necessary to guide treatment for illnesses that are largely self-limited or respond to empiric therapy with erythromycin or tetracycline.

The majority of pneumonias that occur in healthy, ambulatory adults are grouped in the broad classification of the atypical pneumonia syndrome. These infections are relatively homogeneous in their clinical presentation, radiographic findings, and natural history. Nevertheless, they are caused by a wide variety of etiologic agents that include virtually every known type of infectious pathogen such as *Mycoplasma*, bacteria, viruses, *Chlamydia*, rickettsial-like organisms, and even parasites. However, a relatively small number of these agents account for a majority of infections. Of these, *M. pneumoniae* is considered the most common etiologic pathogen. This may reflect the actual frequency of *M. pneumoniae* as a causative agent in the atypical pneumonia syndrome or the relative ease of diagnosis of this infection compared with other possible causes. Recent suggestions that *Legionella pneumophila* and chlamydial species may account for a portion of atypical

cal pneumonia cases underscore the latter possibility. Culture methods and serologic tests have only recently become available to determine the relative incidences of infections with these agents.

Disease caused by *M. pneumoniae* is indistinguishable from disease caused by other atypical pneumonia agents. The course of infection is generally self-limited with or without therapy. Nonetheless, treatment with an antimicrobial agent such as erythromycin or tetracycline has been shown to reduce the duration of symptoms by half [9]. Although infections are generally benign, there have been increasing numbers of reports of fatal cases of *M. pneumoniae* pneumonia in otherwise healthy young adults [10]. *M. pneumoniae* infections have also been associated with a broad array of complicating features, including cases of hemolytic anemia, meningoencephalitis, polyneuritis, and Stevens-Johnson syndrome [11]. Diagnosis of *M. pneumoniae* infection is usually made serologically by increases in titer of cold agglutinating antibody or specific *Mycoplasma* complement-fixing antibody. Antibody titers may take as long as three to six weeks to become elevated.

Other less common causes of the atypical pneumonia syndrome include infections with *L. pneumophila* and other *Legionella* species, influenza A or B, adenoviruses, and chlamydial organisms. It is now apparent that infections with *Legionella*-like organisms have a broad clinical spectrum and occur in distinct epidemiologic settings. The disease spectrum includes the acute upper respiratory presentation of Pontiac fever, self-limited symptoms of an atypical pneumonia, the potentially fatal pneumonia of Legionnaire's disease, and opportunistic pneumonia in immunocompromised hospitalized patients [12–14]. At this time, the percentage of today's cases of atypical pneumonia syndrome due to *Legionella* species is unclear.

Agents responsible for the atypical pneumonia syndrome often are associated with epidemiologic settings that suggest a specific etiologic pathogen, such as a bird fancier with *Chlamydia psittaci* or pneumonia following a visit to areas where coccidioidomycosis or histoplasmosis is endemic. Epidemic pneumonia in a closed population such as a military camp is suggestive of *M. pneumoniae*, *Branhamella catarrhalis*, or adenovirus infection. Legionellosis is suggested by exposure to a potentially contaminated water source. Finally, dry cough and abnormal radiographic appearance in a high-risk patient for the acquired immune deficiency syndrome are highly suggestive of *Pneumocystis carinii* infection.

Fortunately, most cases of atypical pneumonia syndrome are self-limited. Many infections are never recognized or treated and run a benign course. Infections with viral agents such as the influenza viruses, adenoviruses, and measles and varicella viruses are not treatable with specific agents except for the rare case of influenza A virus infection. The primary presentation of histoplasmo-

**TABLE IV Hospitalizations for Pneumonia\***

Age (years)	Number (thousands)	Rate per 1,000 Population	Average Length of Hospital Stay (days)
< 15	229	4.4	5.2
15–44	107	1.0	6.6
45–64	130	2.9	9.4
≥ 65	302	11.5	11.5
Total	768	3.4	8.6

\*First listed diagnosis at discharge (ICD-9-CM code).  
Data from [15].

sis or coccidioidomycosis as an atypical pneumonia also does not require specific antimicrobial therapy. The remainder of the more common causes of atypical pneumonia syndrome are treatable with either erythromycin or tetracycline. When *M. pneumoniae* or *L. pneumophila* is considered the most likely diagnostic possibility, treatment with erythromycin is considered the therapy of choice. When a chlamydial infection is suspected, treatment with tetracycline or one of its derivatives is considered appropriate.

#### COMMUNITY-ACQUIRED BACTERIAL PNEUMONIA

Community-acquired bacterial pneumonias that require hospitalization continue to be a significant cause of morbidity and mortality in the United States, particularly among patients older than 65 years of age. A 1981 National Health Survey reported more than 530,000 hospital admissions for pneumonia for patients older than 15 years of age (Table IV) [15]. Of these, almost 60 percent were for patients more than 65 years of age. The admission rate for this age group was 11.5 cases per 1,000 population per year. In this age group, pneumonia is a significant cause of both morbidity and mortality. The average length of hospital stay for patients older than 65 years of age was 11.5 days and the fatality rate was 12.3 per 100 hospital discharges. Thus, pneumonia remains the "old man's friend" and is frequently reported as a primary cause of death on death certificates. Pneumonia ranks as the sixth leading cause of death in the United States, with a rate of 24.1 deaths per 100,000 population [16]. The only more frequent causes of death are diseases of the heart, malignant neoplasms, cerebrovascular diseases, accidents, and chronic obstructive pulmonary disease.

In the past few years, there has been a growing awareness that the spectrum of agents that cause community-acquired bacterial pneumonia is expanding to include a more diverse group of etiologic pathogens [17,18]. In the preantibiotic era, *Streptococcus pneumoniae* was responsible for the vast majority of community-acquired pneumonias. In the 1960s and early 1970s, the pneumococcus was still considered the most common etiologic pathogen, accounting for 60 to 70 percent of community-acquired cases (Table V) [19,20]. Other agents such as *Staphylo-*

**TABLE V** Causes of Community-Acquired Bacterial Pneumonia in Hospitalized Patients over Past Two Decades

Bacterial Type	Percent of Cases		
	Grady Memorial Hospital 1967-1968 (n = 167)	Milwaukee County General Hospital 1967-1970 (n = 111)	Hartford Hospital 1980-1981 (n = 204)
Streptococcus pneumoniae	62	71	36
Staphylococcus aureus	10	10	8
Hemophilus influenza	8	4	15
Enteric gram-negative organisms	19	13	16
Pseudomonas aeruginosa	1	—	3
Serratia marcescens	—	—	2
Acinetobacter	—	—	1
Legionella pneumophila	—	—	14
Anaerobes/other bacteria	—	3	4

Data from [17,19,20].

coccus aureus, Hemophilus influenza, and enteric gram-negative bacteria were identified in 5 to 20 percent of cases. More recent surveys have identified a much broader array of infectious causes of community-acquired pneumonias. A recent study from Connecticut identified pneumococci as etiologic agents in only 30 to 40 percent of cases [17]. The percent of cases caused by *L. pneumophila*, *H. influenza*, *Pseudomonas aeruginosa*, and other aerobic and anaerobic bacteria has increased.

It is quite likely that some of these new pneumonia agents are actually old bacteria that have been recently rediscovered with the availability of more sensitive culture and serologic methods. It has been documented that Legionella-like agents were present but overlooked as etiologic pathogens in the mid 1960s [21]. The community settings in which pneumonias are occurring are also changing. Antibiotic-resistant organisms are frequently found in nursing homes or other institutional settings in which high-risk patients are clustered. Changing life styles such as promiscuous sexual practices and epidemic drug abuse have created high-risk populations for other pneumonia pathogens such as *P. carinii*. The natural history of certain diseases has also changed. For instance, *H. influenza* was formerly thought to be a disease restricted to pediatric populations; Hemophilus infection is now a relatively common cause of community-acquired pneumonia and a leading cause of pneumonia in smokers with chronic bronchitis. Similarly, respiratory syncytial virus,

which was thought to be primarily a disease of childhood, has now been identified as a cause of adult pneumonia. Even common pathogens such as *M. pneumoniae* are now thought to be responsible for a greater percentage of cases requiring hospitalization. Finally, during the past two decades, several new pulmonary pathogens have been discovered such as *Acinetobacter var. anitratus*, *B. catarrhalis*, *Aeromonas hydrophila*, and an array of new anaerobic pathogens, including *Eikenella corrodens* and *Peptococcus magnus*.

Given the broad spectrum of diagnostic possibilities, there is a greater emphasis on the part of the physician to establish a specific etiologic diagnosis for the more seriously ill hospitalized patients with pneumonia. The clinician may derive important clues from the epidemiologic setting in which the infection occurs, the presence of underlying diseases, the clinical presentation, specific nonpulmonary physical signs, the radiographic appearance, and laboratory abnormalities. However, examination and culture of lower respiratory secretions remain essential to establish a specific etiologic diagnosis. There has been a growing disenchantment with the value of sputum cultures for diagnosis of community-acquired pneumonia [22,23]. Studies have pointed out the lack of value of routinely collected and processed sputum cultures for diagnosis of bacteremic pneumococcal pneumonia. In these studies, pneumococci were isolated from the routinely collected sputum in only 22 to 55 percent of cases. Nonetheless, the value of properly collected and appropriately analyzed sputum samples should not be underestimated. When care is taken to make sure that the specimen is representative of lower respiratory tract purulence, Gram staining and subsequent culture can be extremely valuable in directing appropriate therapeutic decisions. It is noteworthy in the case of the pneumococcus that the organism is relatively fastidious and requires optimal handling to maximize its recovery by culture. In situations in which a sputum sample is unobtainable or results of Gram staining are ambiguous, more invasive techniques must be utilized to obtain a specimen that reflects infection in the lower respiratory tract. In these situations, nasotracheal or transtracheal aspirates are frequently employed if the clinical situation warrants an invasive approach. The frequency of transtracheal aspiration to obtain diagnostic material has declined in recent years because of the fear of complications. Nonetheless, this technique remains a most useful diagnostic bedside procedure in selected patients for whom a specific etiology is needed. Other invasive tests require special equipment and movement of the patient to a bronchoscopy suite, fluoroscopy unit, or operating room. Nonetheless, on occasion, fiberoptic bronchoscopy with lung biopsy under fluoroscopic guidance will provide critical information for diagnosis of a focal pneumonia. Occasionally, open lung biopsy is required to establish a diagnosis. These procedures are especially useful in severely ill, immunocompromised patients in

whom a large number of potentially life-threatening pulmonary pathogens might be responsible for infection and for whom broad-spectrum empiric antimicrobial therapy might not be broad enough to cover all of the etiologic possibilities.

The choice of antimicrobial therapy for an individual case of community-acquired bacterial pneumonia rests with the identification of a specific cause. Traditionally, it has been thought that narrow-spectrum antibiotics were preferable because they had less impact on normal bacterial flora and were less likely to induce bacterial or fungal superinfections. No single agent can cover all of the diagnostic possibilities for even the most simple-appearing community-acquired pneumonia. For the more complex case occurring in an institutional setting outside the hospital or in an unusually susceptible high-risk patient group, even multi-drug combinations may not be broad enough to cover all of the etiologic possibilities. For a severely ill patient with a life-threatening infection, a specific cause must be defined. On the other hand, when the infection is less severe or when specific pathogens are suggested by the epidemiologic setting of the pneumonia, there has

been a growing tendency to prescribe empiric antimicrobial therapy. Thus, patients at high risk for aspiration pneumonia by virtue of the presence of underlying medical disorders are treated with antibiologic agents to cover mixed aerobic and anaerobic infections. Patients from nursing homes with pneumonia are treated empirically for mixed gram-positive and gram-negative pathogens. Less severely ill, young adults with atypical pneumonia syndrome are treated empirically with erythromycin for presumed *Mycoplasma* or *Legionella* infection. Patients with underlying bronchitis or chronic obstructive pulmonary disease receive drugs to cover *S. pneumoniae* and *H. influenzae* as therapy for acute pneumonia. Nonetheless, in each of these situations, it is imperative that appropriate culture specimens of the lower respiratory secretions, blood, or pleural effusion be collected before empiric therapy is initiated. If a specific pathogen is identified, therapy should be modified and the spectrum of coverage narrowed. Cultures also assist the clinician in the diagnosis of the more unusual causes of community-acquired pneumonia that require individualized antibiotic selection on the basis of pathogen identification and sensitivity testing.

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