PNEUMONIA IN THE ELDERLY

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"PNEUMONIA IS THE SPECIAL FRIEND OF OLD AGE".

Osler, 1892.

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I. INTRODUCTION

The demographics of the United States indicate an increasing fraction of elderly citizens. In 1980 22 million persons, or 11% of the population, were over age 65. By the year 2030 it is estimated that this number will approach 17%. An even more dramatic prediction is an increase of persons over age 85 from 2.6 million to greater than 5 million by the turn of the century (1-3).

In 1892 Osler first recognized that pneumonia was both more likely to occur and to cause death among the elderly than among younger persons. In the preantibiotic era the mortality rates for pneumonia were 22% in the third decade, 30% in the fourth, 47% in the fifth, 51% in the sixth and 65% in the seventh (4). Excess pneumonia mortality continues in the elderly even with currently availability of antimicrobial and antiviral agents. It is estimated that persons over 65 years have a five-fold greater mortality than young adults from pneumonia. In the older age group it is the leading infectious cause of death. It has also been estimated that more than $550 million a year is spent on the therapy of bacterial pneumonia in the elderly (3, 5, 6).

The elderly constitute an increasing proportion of both nursing home residents and patients in Intensive Care Units. Elderly residents of chronic care facilities have a reported incidence of pneumonia between two and four times that of the noninstitutionalized (7). Although only 11% of the population is older than 65, they represent the majority of patients in medical intensive care units (8). Additionally, a study carried out in three university affiliated hospitals showed that persons over 60 years were the most frequent patients to develop the adult respiratory distress syndrome (9).

This review is concerned with clinical features of lower respiratory-tract infections in the elderly. The review will first address the age-associated physiologic and immunologic changes that alter the classic clinical presentation of infection.

II. HOST DEFENSE IN THE ELDERLY

A. Colonization

The spectrum of responses to bacteria deposited in the upper and lower respiratory tracts varies from total clearance to overwhelming infection. Colonization is intermediate between these extremes and can be defined as persistence and growth of microorganisms on a mucosal surface in the absence of infection.

Studies of colonization rates of the elderly are limited, but it is clear that oropharyngeal colonization with gram negative bacilli increases with age (Table 1) (10).

Table 1

Oropharyngeal Colonization With Gram Negative Aerobic Bacilli Among Retirement Community Residents

Retirement Community	
Independent apartments	20%
Assisted care	23%
Debilitated	42%
Critically ill (Infirmary)	60%
Controls	
Normal adults <65 y/o	8%

Studies of older persons in a retirement community indicate an increased rate of colonization with gram negative bacilli both with age and with severity of illness ranging from 20% of healthy elderly persons to 60% of older patients with critical illness compared to 8% of normal younger persons. Colonization has been specifically associated with extent of chronic illness, bladder incontinence, chronic cardiac or respiratory disease, use of antacids, and deteriorating level of activity. Analysis of these data suggest that the extent to which an older patient is bedridden correlates with colonization.

The gram negative bacilli isolated include Klebsiella species in 41%, Escherichia coli 24%, Enterobacter species 14% and Pseudomonas aeruginosa and Proteus mirabilis in approximately 5% each. Pseudomonas and Proteus occur only in patients that are debilitated and housed in a skilled nursing environment. Up to 90% of these patients have a single species of gram negative bacilli isolated from their oropharyngeal cultures. These findings are supported by similar findings by Pierce and colleagues and have therapeutic implications (11). It has also been found that colonization of the oropharynx precedes the onset of pneumonia in 85% of critically ill individuals (12).

Data on colonization with gram positive bacteria are not available, although one study suggests an increased incidence of staphylococcal pneumonia in aged persons (13).

Although the elderly are more frequently colonized with pathogenic bacteria, the presence of bacteria alone does not predict the occurrence of infection if host defenses are intact. However, host defenses are not intact in this age group.

B. Host Defense Impairment

Age related alterations predisposing to pneumonia may be divided into changes in lung structure and changes in the immune system. Lung structural changes are well described and are listed in Table 2 (14).

Table 2

Lung Structural Changes in the Elderly
Which Decrease Host Defense

Decreased elasticity
Ineffective cough
Decreased mucociliary clearance

With advancing age the lung loses elasticity leading to an increase in functional residual capacity. Pulmonary function tests demonstrate mild airflow obstruction in small airways. Impairment of arterial oxygenation due to increased shunting and ventilation perfusion ratio imbalance have been attributed to small airways closure during normal ventilation. Additionally, these changes may contribute to decreased cough effectiveness which results in a decreased clearance of microorganisms from the respiratory tract.

Mucociliary clearance is also impaired in both smoking and nonsmoking elderly persons when compared with younger individuals. The etiology of this alteration is unclear but has been related to both the nature and distribution of airway secretions and the number of epithelial and mucous producing cells (15).

Changes in the immune system with age have also been investigated and are listed in Table 3.

Table 3

Changes of the Immune System in the Elderly
Which Decrease Host Defense

Anatomic changes
Lymphocyte changes
Humoral immunity
Cell-mediated immunity

The involution of the thymus gland is the most dramatic and universal age-associated change in the anatomy of the immune system. This involution is associated with a decline in serum thymic hormone activity which becomes undetectable in normal persons over the age of 60 (16). In addition there is loss of the thymic microenvironment that facilitates the differentiation

of T lymphocyte precursors formed in the bone marrow. Thus, fewer precursors enter the thymus and fewer thymocytes differentiate into mature T cells (17-19).

In contrast to thymic involution, there are opposite changes in other lymphoid tissues. For example, the number of germinal centers within lymph nodes increase, and there are increases in plasma cells and lymphocytes within the bone marrow (20).

The total number of blood lymphocytes does not change with age. However, there are modest but consistent changes in the distribution of blood T lymphocyte subsets. The number of immature T cells and CD_4 bearing T cells increases, while the number of CD_8 bearing T cells decreases (20, 21).

Alterations of humoral immunity with age was first demonstrated over fifty years ago (22-24). A summary of the alterations of humoral immunity reported with age is listed in Table 4.

Table 4

Humoral Immunity Alterations With Age

Response to foreign antigens	↓
Number of lymphocytes	NC
Concentration of immunoglobulins	NC
Number of antibody producing cells	NC
Amount of antibody	NC
Autoantibodies	↑

Antibody response to foreign antigens is both quantitatively and qualitatively impaired in the aged. However, the number of lymphocytes, the concentration of serum immunoglobulins, the total number of antibody producing cells and the total amount of antibody formed are generally unaltered. Conversely, autoantibodies increase with age. Thus, aging is associated with a decreased production of antibody to foreign antigens and a concomitant increase in antibody to self antigens, and the same over-all level of immunoglobulin synthesis (25).

Cell-mediated immunity depends on the functional integrity of thymic dependent lymphocytes. As thymic involution is a universal accompaniment of aging, many studies of immune senescence have focused on T lymphocyte function. A summary of the alterations in cell mediated immunity with age are listed in Table 5.

Table 5

Cell-Mediated Immunity Alterations With Age

Cell-mediated immunity	↓
Number of T cells	NC
Responsive T cells	↓
Proliferation capacity	↓
Production of IL 2	↓
Response to IL 2	↓

Cell-mediated immunity is markedly impaired in older persons. Although the total number of T cells remains unchanged there is a impaired proliferative response resulting from a decrease in the number of responsive T cells as well as an impaired proliferative capacity of the remaining responsive T cells. The failure of activation can be attributed to a decrease response of nuclei in old lymphocytes to cytoplasmic signals that initiate DNA replications. There is decreased production of and response to the T cell growth factor IL 2 by T cells from older individuals. These two changes combine to contribute to the decreased response of T cells to mitogen (26-30).

Thus, immune senescence leads to a moderately immunodeficient state in which opportunistic infections do not generally occur. However, the impairment of cell-mediated immunity can be directly associated with the activation of the varicella virus and to the increasing incidence of Mycobacterium tuberculosis in the aged population. Likewise it is assumed that the sum of the alterations in immune responses contributes to the increased attack rate and mortality from pneumonia.

III. CLINICAL FEATURES OF AEROBIC BACTERIAL PNEUMONIA IN THE ELDERLY

A. Signs and Symptoms

Osler first noted that signs and symptoms may be incompletely expressed in the elderly patients with pneumonia. "In old age, pneumonia may be latent, coming on without chill. The cough and expectoration is slight, physical signs ill defined and changeable, and the constitutional symptoms out of all proportion. Of fever there may be none. Fever is higher in healthy adults than in old persons and drunkards" (4). Contemporary studies have confirmed this original description and have associated increasing atypia of signs and symptoms with an increased mortality. Table 6 presents the historical data from patients with a mean age of 82.5 years (31-33).

Table 6

Clinical Features of Aerobic Bacterial Pneumonia in Elderly Patients

History	Pts. <65 yrs. n=57	Pts. >65 yrs. Survivors n=69	Pts. >65 yrs. Deaths n=31
Chills (rigors)	55% (18%)	32% (9%)	10%
Fever	74%	28%	13%
Cough	82%	73%	61%
Increased sputum	66%	58%	45%
Chest pain	48%	35%	32%
Dyspnea	-	75%	55%

The classic history of aerobic bacterial pneumonia obtained in younger patients is the abrupt onset of chills, which may be true rigors, fever, cough productive of purulent sputum, and pleural chest pain. The data presented in Table 6 indicate that the majority of persons under 65 years have each of these symptoms. Older patients are much less likely to give a history of these events, especially a history of chills, fever, and chest pain. However, pneumonia more frequently presents with dyspnea in the elderly. It is also striking that the "classic" symptoms were even less common in patients with a fatal outcome. Indeed 10 patients had no cough, dyspnea, sputum production or chest pain. Of additional interest is the fact that a quarter of elderly patients reports falling as a part of the symptom complex.

Table 7 presents the physical signs at presentation found in the same group of patients.

Table 7

Clinical Features of Aerobic Bacterial Pneumonia in the Elderly

Signs	Pts. <65 yrs. n=57	Pts. >65 yrs. Survivors n=69	Pts. >65 yrs. Death n=31
Resp. rate >26/min.	-	57%	74%
Pulse >100/min.	-	22%	45%
Temperature >37.8°	74%	28%	13%
Acute confusion	16%	30%	65%
Bronchial breath sds.	36%	22%	39%
Rales	79%	88%	94%

Respiratory rate is increased but tachycardia is not common in the elderly. As described by Osler the absence of fever is

common and is associated with increased mortality. Acute confusion is an important clinical sign in this age group and has been reported by others to occur in between 47 and 65% of elderly patients. This sign has also been reported as the only manifestation of pneumonia in a small number of patients, particularly those confined to a nursing home (34). Similar to younger patients signs of consolidation are present in less than a third of elderly patients, whereas rales are almost always detectable. The high incidence of rales in this study may be spurious due to simultaneous congestive heart failure.

B. Laboratory Features

The leukocyte count is similarly unpredictable as presented in Table 8 (35).

Table 8

White Blood Cell Count In
Elderly Patients with Pneumonia

WBC count	
<10,000	31%
10-15,000	38%
>15,000	31%
PNM + bands	
<80	27%
≥80	73%

Harper found that leukopenia, leukocytosis and a normal WBC count each occurred in a third of elderly patients admitted to a VA Hospital. Although the total count was inconsistent a shift to polymorphonuclear leukocytes and bands occurred in greater than 80%. The WBC count did not correlate with age, maximum temperature, serum albumin, number of medical problems or number of medications.

No other laboratory exam has been found to be useful in the diagnosis of aerobic bacterial pneumonia in the elderly.

C. Radiography

The chest radiograph usually reveals an infiltrate at the time of presentation. The contrasting features in younger and older persons which have been reported are presented in Table 9 (3, 32, 36, 37).

Table 9

Radiographic Features of Aerobic Bacterial Pneumonia in the Elderly

Finding	<65 yr.	>65 yr.
Incomplete consolidation	50%	65%
Infiltrate >1 lobe	22%	48%
Effusions	9%	25%
Cavitation	-	5%
Progression of infiltrates	9%	48%
Resolution	6 wks	>14 wks

Incomplete lobar consolidation is more common in older than in younger persons. The high prevalence of bullae and COPD in this age group likely accounts for this finding. Two or more lobes are involved at the time of diagnosis in about half of the elderly patients compared to 22% of those under 65; this finding apparently results from a later presentation due to less striking symptoms. Pleural effusions are also significantly more common, but an increased occurrence of empyema is less well documented. Cavitation is distinctly uncommon.

Radiographic progressions of infiltrates after treatment with appropriate antimicrobials is uncommon in younger persons with pneumococcal pneumonia, but up to half of persons >65 years exhibit this phenomenon. Additionally, resolution of infiltrates is slow (38). In a study by Jay of 72 survivors of bacteremic pneumococcal pneumonia, delayed resolution occurred in those >50 years and in those with underlying COPD. In each of these groups 60% of radiographs were still abnormal at 14 weeks, while 100% of persons <50 years had resolution in 6 weeks (39).

IV. USUAL AEROBIC BACTERIAL ETIOLOGIES

Appropriate antibiotic therapy of aerobic bacterial pneumonia dictates a knowledge of the causative organisms. The frequency of diagnosing the specific bacterial etiology of pneumonia has been investigated by age group, and the results are presented in Table 10 (40).

Table 10

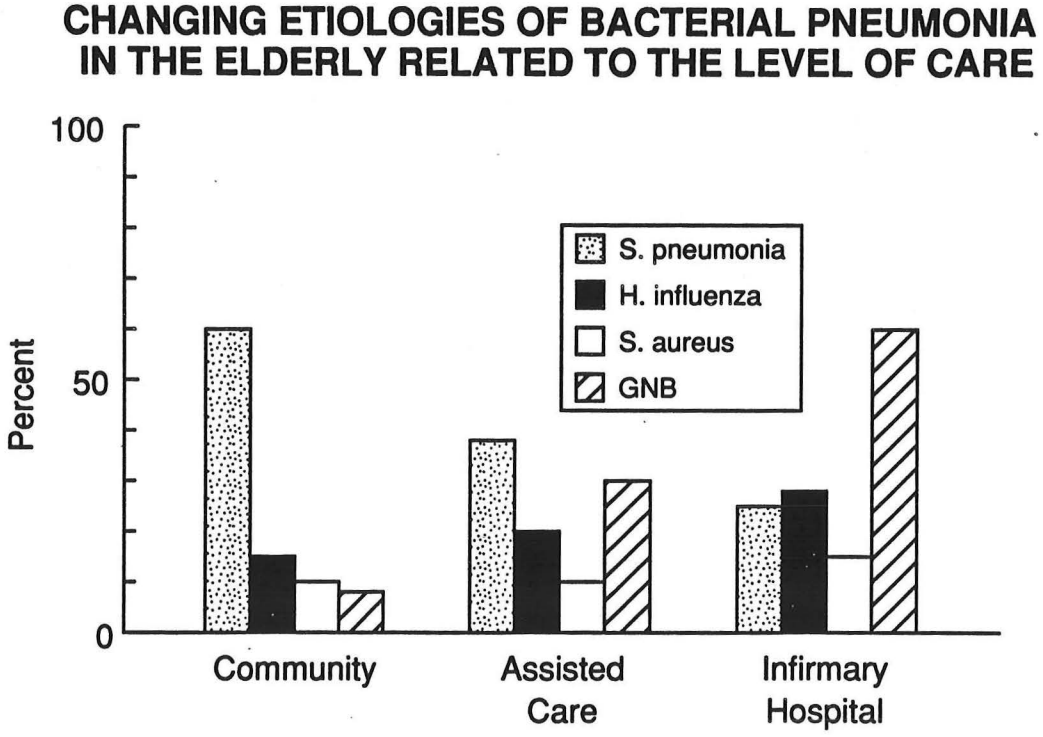
Frequency of Diagnosing the Specific Cause of Bacterial Pneumonia by Age Group

Infectious Agent	Age Group 20-40 n=24	41-64 n=49	>65 n=33
Unknown	37%	47%	54%
Specific bacterial etiology	63%	53%	46%

As indicated in this study, the specific bacterial etiology of an episode of pneumonia is not diagnosed in about 40% of younger patients, and the diagnosis rate further decreases with age. Thus an estimate of the best antimicrobial agent for therapy is based on which organisms are most likely in a particular clinical setting.

The overall incidence of the bacterial etiologies of pneumonia in the elderly have been clearly related to site of residence and the degree of host impairment and correlate with oropharyngeal colonization (Figure 1) (41).

Figure 1



Garb, J.L., et al: JAMA 240:2169, 1978.

The cause of bacterial pneumonia in young healthy persons is almostly always Streptococcus pneumoniae. Even in normal elderly persons living independently without assistance pneumococcus causes a lesser but still significant fraction of aerobic bacterial pneumonias, approximately 40-60% (40, 42). In elderly patients pneumococcal bacteremia is more frequent and is associated with a higher mortality than younger patients. In the age group >90 years bacteremia with this organism has an 83% mortality rate (5, 43).

Haemophilus influenzae pneumonia occurs in approximately 15% of community based elderly patients (6, 44). This organism is especially common in patients with chronic obstructive lung disease among whom the oropharynx is colonized up to 60% of the time (45, 46). Type B encapsulated strains are more likely to be bacteremic than Streptococcus pneumoniae; however non-typeable strains, which are rarely bacteremic, are more common in the elderly, occurring in 85% of samples with Haemophilus influenzae obtained by transtracheal aspiration (47).

Staphylococcus aureus pneumonia has been documented in approximately 10% of community based patients. As in the younger population this pathogen most frequently occurs during an influenza epidemic. Other clinical features unique to the older population have not been described with the exception of an increased mortality rate, 50% compared to 25% in a younger group (48). Radiographic findings do not include the nodular hematogenous pattern found in intravenous drug abusers.

The incidence of community acquired gram negative bacillary pneumonia is small but significant in older age patients. Of all gram negative pathogenic bacteria isolated Klebsiella pneumoniae is the most common being found in 9% of isolates. Escherichia coli, Enterobacter aerogenes, and Proteus mirabilis occur in 8%. Pseudomonas aeruginosa, Serratia marcescens, Citrobacter and Acinetobacter calcoaceticus are distinctly uncommon, found in less than 2% (41). Severity of illness with features of a necrotizing process such as blood tinged sputum, hypotension, severe hypoxemia and confusion are no different from younger patients. Gram negative bacillary infections in community patients correlate well with general debility even when residing in a home environment (49, 50).

As patients require a higher level of care the bacterial etiologies of pneumonia change significantly. In assisted care facilities pneumococcal pneumonia decreases to approximately 38% of infections, Haemophilus influenzae increases to 20% and Staphylococcus aureus remains unchanged at 10%. However, even in a low assisted care facility gram negative bacillary pneumonias due to Klebsiella pneumoniae, Escherichia coli, or Enterobacter aerogenes increase markedly to approximately 30% (40-42).

As the elderly become confined to either a skilled care nursing home or are admitted to a general hospital the change in

bacterial etiology is again dramatic. In these situations Streptococcus pneumoniae is seen in only a quarter of the patients. Haemophilus influenzae has increases to almost 30%, and Staphylococcus aureus increases slightly in incidence to 15%. Staphylococci and non-typeable Haemophilus influenzae are being increasingly reported as the etiology of nosocomial pneumonia in these patients (41).

Gram negative bacillary pneumonia comprises about 60% of cases. Klebsiella pneumoniae continues to be the predominate GNB isolated occurring in 40% of specimens. Escherichia coli, Enterobacter aerogenes and Proteus mirabilis occur in 20% and Pseudomonas aeruginosa, Serratia marcescens and Citrobacter in 10%. Acinetobacter species remains a minor pathogen occurring in less than 5% of isolates (41).

Mixed microbial infections, as judged by sputum isolates, have been investigated and are apparently more common over the age of 65; multiple isolates also increase with increasing debility and level of care (33, 51).

Clinical features associated with the different bacterial etiologies are the same as those in patients with community acquired disease.

V. THERAPY OF USUAL AEROBIC BACTERIAL PNEUMONIA IN THE ELDERLY

When considering antimicrobial therapy for aerobic bacterial pneumonia the clinician should be aware of age related physiologic changes that alter drug metabolism and enhance susceptibility to the toxic effects of antimicrobials. These changes are listed in Table 11.

Table 11

Age Related Changes
that Effect Drug Metabolism

Body water	↓
Lean body mass	↓
Body fat	↑
Muscle mass	↓

With aging there is a reduction in total body water and in lean body mass and an increase in body fat resulting in a decreased volume of drug distribution. Thus both blood and tissue concentrations of drugs may be higher than predicted (52). The decreased muscle mass also may result in a lower serum creatinine than would be expected from the patient's true level of renal function. When the serum creatinine concentration is used to calculate the dose of an aminoglycoside, a higher than expected peak serum aminoglycoside level occurs. High peak serum

concentrations have been associated with excessive nephrotoxicity in older compared to younger patients with the same peak levels (53, 54). Thus, monitoring of peak and trough concentrations and careful adjustment of dosage to include volume of distribution calculations are necessary in this age group.

In patients with a history of congestive heart failure one should also be aware of the variable sodium content of the parenteral antimicrobials listed in Table 12.

Table 12

Sodium Content of Parenteral Antibiotics
on the Parkland Formulary in mEq/Gm

Aztreonam	0	Cefuroxime	2.4
Carbenicillin	4.7-6.5	Imipenem	3.2
Cefazolin	2.0	Methicilin	2.6-3.1
Cefotaxime	2.2	Mezlocillin	1.85
Cefotetan	3.5	Nafcillin	2.9
Cefoxitin	2.3	Piperacillin	1.85
Ceftazidime	2.3	Ticarcillin	5.2-6.5
Ceftriaxone	3.6	Ticarcillin/ clavulanate	4.75

Ticarcillin has the highest sodium content with approximately 6 meq/gm of drug. The usual dosage of Ticarcillin is 12 gms per day resulting in a patient receiving 72 meq of sodium from the drug alone. The compound can be mixed with normal saline or dextrose and water for injection. When saline is used the drug is diluted with 50 ml of normal saline resulting in the patients receiving a total of 100 meq/day of sodium. A liter of normal saline contains 154 meq of sodium so that treatment with this drug is equivalent to infusing at least a half liter of normal saline. In patients with a history of congestive heart failure alternative treatment should be considered with knowledge of the sodium content.

Since knowledge of the specific organism causing an aerobic bacterial pneumonia is even less likely than in younger persons, antimicrobial therapy is empiric and dictated by knowledge of colonization, host impairment and the clinical setting.

Recommendations for empiric treatment of elderly patients living in the community are found in Table 13.

Table 13

Treatment of Aerobic Bacterial Pneumonia
in the Community Based Elderly

TMP/SMX
TMP/SMX + Nafcillin
Cefotaxime, Ceftriaxone
Ampicillin/sulbactam
Ticarcillin/clavulanate
Amoxicillin/clavulanate

The organisms causing pneumonia in the elderly who are community based are similar to the organisms in younger patients. Differences include fewer cases due to Streptococcus pneumoniae and more cases due to Haemophilus influenzae; the latter are frequently unencapsulated, non-typeable β lactamase producing strains. There are also a small number of patients with the common gram negative bacillary organisms (40, 43, 50). Pseudomonas and other non enteric gram negative bacilli account for less than one percent of pneumonia in these patients. Trimethoprim sulfamethoxazole has broad spectrum coverage that includes the pneumococcus, β lactamase producing Haemophilus influenzae and the common gram negative bacillary organisms including Klebsiella pneumoniae, Escherichia coli, and Enterobacter aerogenes. Depending on degree of illness the drug can be given orally or IV. Staphylococcal activity is only moderate with this drug, and it should be used in combination with Nafcillin when there is influenza in the community. Community acquired methicillin resistant staphylococcal pneumonia has not been reported in this age group.

A pneumococcus resistant to Trimethoprim sulfa was first reported in 1972 and an incidence of 8.7% resistance to Trimethoprim sulfa occurred in Israel in 1983. Resistant strains have occurred in the Dallas area; the exact incidence is not known but believed to be low. In a study of 26 consecutive patients performed in 1986 at Parkland Hospital the drug was efficacious when administered intravenously in 100% of patients with community acquired pneumonia. Ninety percent of the study group were infected with Streptococcus pneumoniae. At usual intravenous dosage the cost to Parkland is $4.50 per day and in the era of cost containment this regimen is the most economic.

In patients sensitive to sulfa containing compounds a third generation cephalosporin is recommended because of activity against β lactamase producing organisms. First and second generation cephalosporins do not have comparable activity. Cefotaxime and ceftriaxone provide a similar spectrum to TMP/SMX, but at Parkland Hospital ceftriaxone is double the cost of cefotaxime given in appropriate doses. Cifixime is the only third generation cephalosporin available for oral administration; it's cost is over $4.50/day to Parkland.

A third choice of antimicrobials in these patients is a combination of a β lactamase inhibitor and β lactam agent. Ampicillin/sulbactam and Ticarcillin/clavulanate have a clinical efficacy similar to the third generation cephalosporins. These agents have equal effectiveness in treating infections with Streptococcus pneumoniae, Haemophilus influenzae including β lactamase positive organisms, nonmethicillin resistant Staphylococcus aureus and the usual gram negative bacilli. Ticarcillin clavulanate has the advantage of activity against Pseudomonas aeruginosa and Serratia marcescens with a cost that is more than double Ampicillin sulbactam. If infection with these organisms is clinically suspected empiric treatment should follow the recommendations for those living in an assisted care facility or a nursing home.

Recommendations for empiric treatment of elderly patients residing in an assisted care facility or in a skilled nursing home or hospital setting are given in Table 14.

Table 14

Treatment of Aerobic Bacterial Pneumonia in Patients in Either the Assisted Care or Infirmary Groups

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Mezlocillin + Gentamicin or + Tobramycin

Ceftazidime + Gentamicin or + Tobramycin

Since patients residing in assisted care facilities have a 30% incidence of gram negative bacillary pneumonia it is reasonable to begin empiric treatment to cover all organisms that occur in the infirmary or nursing home acquired group. Although outcome of empiric monodrug therapy of nursing home patients with pneumonia has sometimes been equivalent to that with combination regimens (55-57), there have been emergence of antibiotic resistant bacteria and also serious bacterial superinfection with this approach (58-60). Additionally, the use of monodrug regimens may not result in optimal Pseudomonas aeruginosa coverage which may occur in up to 10% of these patients. Numerous reports have described both in vitro and in vivo synergism for β lactam/aminoglycoside combinations against isolates of Pseudomonas aeruginosa (61-65).

Equal efficacy for empiric treatment of these patients includes an antipseudomonal penicillin such as mezlocillin, the most economic approach, or a third generation antipseudomonal cephalosporin such as Ceftazidime for penicillin sensitive patients. Either antimicrobial is combined with an aminoglycoside.

The empiric choice of an aminoglycoside should be gentamicin to which most strains of Pseudomonas aeruginosa are sensitive.

The cost to Parkland Hospital for gentamicin is $0.26 per 80 mgm versus $4.25 for tobramycin. The latter is used only in the case of organisms proven resistant to gentamicin. The third aminoglycoside, amikacin costs $50.76/500 mgm and has no specific advantage in treating pneumonia unless organisms are demonstrated to be resistant to both of the other aminoglycosides.

Both of these regimens will treat staphylococcal disease that is not methicillin resistant. If methicillin resistant staphylococci are known to occur in the nursing facility, vancomycin should be added to the original regimen.

VI. UNCOMMON AEROBIC BACTERIAL ETIOLOGIES

Pneumonias due to uncommon aerobic bacteria have special significance in the elderly and are listed in Table 15.

Table 15

Uncommon Bacterial Pneumonias
Occurring in the Elderly

β hemolytic streptococci-Group A and B
Branhamella catarrhalis
Legionella pneumophilia

In recent years both Group A and B β hemolytic streptococcal infections in adults have been increasingly reported in the United States (8, 66-70). Group A infections reported to the CDC occurred as nosocomial outbreaks in nursing homes in Illinois, Kansas, North Carolina and Texas. A majority of the patients had severe pneumonia with ARDS, and there was a 56% mortality rate. Clinical features included symptoms of severe pneumonia and skin rash with or without a toxic shock-like syndrome. The CDC predicts additional outbreaks due to the propensity of the organism to cause disease in the elderly and the ability of the organism to spread from person to person (71). Likewise, Group B β hemolytic Streptococcal pneumonia has been reported in the elderly. The mean age of cases was 73 years, and there was a 100% mortality. The clinical picture was a severe pneumonia with frequent early empyema and the findings of necrotic, pus containing sacs at autopsy. There were no skin lesions or toxic shock-like syndrome. Most are nosocomial infections that occur in the most debilitated patients (72). Previously recommended antimicrobials all adequately cover streptococcal disease.

Branhamella catarrhalis, previously named Neisseria catarrhalis, has been considered to be a nonpathogenic commensal of the upper respiratory tract (73). Recent investigations have documented its pathogenicity and described the clinical characteristics of pneumonia caused by this organism (Table 16) (74-77).

Table 16

Clinical Characteristics of Pneumonia Caused by Branhamella catarrhalis

Parameter	Percent
Age >65 years	50-70
COPD	52-83
Peak temperature >38°	50
WBC >20 K/mm^3	17
Non-consolidating infiltrate	50-70
Pleural effusion, cavitation	0
Positive blood culture	4
β lactamase positive	50-70

In all series reported Branhamella pneumonia has occurred predominantly in those over 65 years. There is a high association with chronic obstructive lung disease, up to 83% of patients in one series. Each series emphasizes the paucity of clinical symptoms. Half of the patients are afebrile and have only mild cough, dyspnea or weakness. A normal WBC count occurs in 50% and is rarely over 20,000/mm^3; however there is a shift to immature band forms like that seen in the usual aerobic bacterial pneumonias. Chest radiography shows the incomplete consolidation characteristic of patients with underlying COPD (36). Pleural effusion and cavitation have not been reported. Blood cultures are rarely positive and mortality is low ranging from 0-7%. Most organism are β lactamase positive but should respond to the treatment regimens recommended for usual community acquired aerobic bacterial pneumonia in the elderly.

Diagnosis of infection with this organism is suspected by seeing gram negative diplococci in WBC's in sputa but can be made with certainty only retrospectively by demonstration of a bactericidal IgG antibody in convalescent serum. The antibody has occurred in >90% of patients in the convalescent phase (77, 78).

Pneumonia secondary to Legionella pneumophilia was first described in 1976 in epidemic form (79). Since that time it is clear that sporadic cases also occur, predominantly in elderly male smokers (80). The prevalence of sporadic cases varies markedly in different geographic locations. In Pittsburgh this organism has been reported in up to 23% of all cases of community acquired pneumonia, whereas in Seattle the prevalence has been found to be only 1% (81, 82). The prevalence in Dallas is similar to Seattle. Additionally, only 2% of nursing homes residents have been demonstrated to have significant antibody titers (>1:64) to the organism (83). The common clinical features listed in Table 17 are severe in the elderly (83).

Table 17

Clinical Features of Legionnaires Disease in the Elderly

Abrupt onset malaise, headache, myalgia, weakness
Fever, bradycardia
Purulent sputa, hemoptysis
Abdominal discomfort, watery diarrhea
Change in mental status

Clinical features of pneumonia caused by this organism specifically in elderly patients have rarely been addressed. However given the excess mortality rate in the aged population an excess severity of symptomatology has been assumed (83-85). As in younger persons the onset is abrupt and is usually severe malaise, headache, myalgias and weakness. Fever with a relative bradycardia is more common than in patients with usual aerobic bacterial pneumonia. Purulent sputa with hemoptysis are reported in up to one-third of patients. Abdominal discomfort with watery non-bloody diarrhea occurs in approximately 50%. Change in mental status including confusion, lethargy, depression, hallucinations, delirium and amnesia are considerly more common in older persons than younger persons and have been reported in excess of 75% of such patients (83).

Laboratory features listed in Table 18 are similar to those found in younger patients.

Table 18

Laboratory Features of Legionella pneumophila Pneumonia in the Elderly

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Gram stain-leukocytes without organisms
Hyponatremia
Liver function abnormalities

Seventy-five percent of patients ultimately develop purulent sputum with numerous leukocytes without stainable organisms (86). Hyponatremia (serum Na$\leq$130 neg/L) is more common in Legionella pneumophila pneumonia than in usual aerobic bacterial pneumonia. Liver function abnormalities are frequent but non-specific and not a useful tool in the differential diagnosis. There are no specific radiographic features associated with this organism (87). Thus there are no clear distinguishing features of Legionella pneumophilia pneumonia in the elderly.

The organism has not been reported as a epidemic cause of pneumonia within a nursing home or retirement community (86) and there is a low incidence of seropositivity in elderly patients in these settings. Thus, this organism is likely an infrequent problem, particularly in our area (80). Nevertheless, in a

patient with pneumonia with prominent symptoms of diarrhea and acute confusion out of proportion to the degree of hypoxemia, especially if associated with hyponatremia, this diagnosis should be considered. A direct fluorescent antibody test performed on sputum can rapidly suggest the correct diagnosis. The test is highly specific (>90%) although relatively insensitive (25-80%). Positivity depends of the presence of a large burden of organisms and crossreactions have been reported to Bacteroides fragilis, Pseudomonas species, Flavobacterium and Xanthomonas species. If the direct fluorescent antibody test is positive, or if negative and a high clinical suspicion remains, coverage should be broadened to include erythromycin. If erythromycin is not tolerated rifampin has also been demonstrated to have in vitro and in vivo efficacy. Trimethoprim sulfamethoxazole has also been used successfully in patients with Legionnaires' disease and with Legionella micdadei that failed to respond to erythromycin (88, 89).

VII. ATYPICAL PNEUMONIA IN THE ELDERLY

A. Magnitude of the Problem

The term primary atypical pneumonia was originally used to denote a pneumonia that presented without the characteristic clinical and radiographic features of aerobic bacterial pneumonia. When it was realized that the syndrome was caused by more than one etiologic agent the term "primary" was dropped, and the term atypical pneumonia is now used for clinical findings suggesting a nonbacterial pneumonia.

Atypical pneumonia is generally not considered in the differential diagnosis of pneumonia in the elderly. This omission is not based on available data. The prevalence of age related viral and mycoplasma infection was first addressed by Mufson in 1967 (Table 19) (90).

Table 19

Age Related Evidence of Viral and Mycoplasma Infection

	% CF Titer Rise						
Age (yrs)	20-29	30-39	40-49	50-59	60-69	70-79	80-99
n	32	88	116	78	50	32	23
Viral	25%	15%	6%	13%	24%	36%	42%
Mycoplasma	15%	10%	5%	6%	3%	14%	18%

Three hundred forty six patients with radiographic evidence of pneumonia, 105 over the age of 60, were studied with

serological tests for viruses and mycoplasma. Patients in the viral infection group demonstrated a four-fold rise in complement fixing antibodies to either influenza A or B, parainfluenza Types 1, 2 or 3, adenovirus or respiratory syncytial virus. Mycoplasma infections were similarly indicated by antibody titer rises to Mycoplasma pneumoniae or Mycoplasma hominis Type 1. The percent of patients with pneumonia apparently due to virus was highest in young and old adults and least in middle aged adults. Mycoplasma infection was much less common but showed the same trends. These data certainly suggest that atypical pneumonias due to viruses or mycoplasma are common in the elderly.

More recent studies performed both on nursing home residents and community based elderly support a significant viral infection rate (Table 20) (33, 91, 92).

Table 20

Viral Infection Rate in the Elderly

	% CF Titer Rise or Viral Isolation			
	Influenza A or B	Respiratory Syncytial Virus	Parainfluenza Virus	Adenovirus
Morales n=125	23	9	-	-
Freeman n=40	25	12	10	9
Marrie n=51	14	2	8	-

Morales and Freeman studied respiratory infection in 165 nursing home residents with a mean age of 79 years. A causative agent was assumed to be present by demonstrating either a four-fold complement fixing antibody titer rise, viral isolation or both. Respiratory infection was attributed to influenza A or B in one quarter and to respiratory syncytial virus in approximately 10%. Additionally, Freeman reported an approximate 10% infection rate due to each parainfluenza and adenovirus. In 51 patients with a mean age of 77 years Marrie demonstrated an overall viral etiology of 40% in elderly patients hospitalized for community acquired pneumonia. Influenza infections were the most frequent at 14%; however, cytomegovirus and herpes simplex virus were also thought to be the cause of some infections.

These studies support the concept that viruses cause a significant percentage of the pneumonia seen in elderly patients.

B. Influenza

Influenza A or B infection is the most frequent and most severe of the atypical pneumonias among elderly persons (93-95). The overall attack rate among the community based elderly has been related to the home environment (Table 21).

Table 21

Influenza A Attack Rates in Families With and Without School Children

Age in Years	With School Children	Without School Children
0-4	34%	29%
15-39	34%	18%
40-59	32%	17%
>60	31%	10%

In this study families with school age children had an attack rate of approximately 30% regardless of age. The attack rate decreased to a low of 10% in those persons over 60 years of age living in families without children. I interpret these data to mean that Influenza A infection in the community based elderly is unlikely to occur without significant exposure to a younger age group that is a known reservoir of infection. In contrast to community based persons, attack rates among elderly nursing home residents have been between 50 to 60% and vary with the percentage of vaccinated persons (96-99). History of an influenza like respiratory illness occurring in a nursing home facility is the single most important feature in making this diagnosis.

As in aerobic bacterial pneumonia clinical symptoms of influenza in the older persons differs from those seen in younger persons (Table 22) (96, 99, 100).

Table 22

Clinical Features of Influenza With or Without Pneumonia in the Elderly

Feature	10-49 yrs. n=77	60-80 yrs. n=47
Cough	18%	55%
Cough, headache	16%	30%
Cough, myalgias, headache	25%	6%
Cough, myalgias, headache, sore throat	25%	2%
Vomiting	17%	4%

In a large study from Australia 333 cases of influenza were documented by isolation of the virus, and symptoms were recorded by age group. The total classic complex of cough, myalgias, headache and sore throat was found in only 2% of persons between the ages of 60 and 80, whereas cough alone or cough with headache occurred in 85%. Only a third of young persons reported cough alone or cough with headache as the only symptoms. Gastrointestinal symptomatology also decreased with advancing age. Altered mental status with acute confusion was frequently noted in all studies of influenza in the elderly but the frequency is undocumented.

Physical and laboratory findings of uncomplicated influenza in the elderly are less well documented. Available data are presented in Table 23 (92).

Table 23

Clinical and Laboratory Features of Influenza in 40 Elderly Patients

Feature	Percent
Respiratory rate >20/min	71
Pulse >90/min	35
Temperature >37.8°	24
Leukocytosis	24

Patients in this study had a mean age of 79 years with a range of 63 to 96. Physical and laboratory findings were similar to aerobic bacterial pneumonia and emphasize an increased respiratory rate as the most consistent finding of influenza in the older age group. Pyrexia, tachycardia and leukocytosis were uncommon.

Because of underlying chronic disease elderly patients may be predisposed to the syndrome of influenza pneumonia, first clearly described by Louria in 1959 (101). The clinical features of this disease listed in Table 24 are dramatic and apparently not age related (101-103).

Table 24

Clinical Features of Influenza Pneumonia
in 31 Patients

Feature	Percent
Sudden onset	80
Dyspnea	90
Cough	100
Hemoptysis	80
Fever >38.8°	84
Chest pain	15

In thirty one cases of well documented influenza pneumonia the age range was 11 to 75 years with 45% of patients over age 45. Symptoms were the same in all age groups. There was most often a dramatic, sudden onset of flu-like symptoms followed by progressivly severe dyspnea. All patients experienced cough, and hemoptysis occurred in 80%. Fever of >38.8°C was common, but hypothermia was also reported. Pleuritic chest pain was uncommon.

The signs of influenza pneumonia listed in Table 25 were also indicative of severe illness.

Table 25

Clinical Features of Influenza Pneumonia
in 31 Patients

Feature	Percent
Tachypnea >30 minutes	91
Cyanosis	93
Tachycardia >110	80
Shock	44
Rales	97
Leukocytosis >11,000	52
Mortality	94

Tachypnea with markedly increased minute ventilation and cyanosis were consistent features at time of presentation. Tachycardia was present in the majority, not uncommonly associated with peripheral circulatory collapse. Moist rales sometimes, associated with wheezing was reported in 97% of patients. Leukocytosis with a shift to immature forms occurred in 52%. There was a 94% mortality, most commonly occurring in the 72 hours following admission. Most patients in these early series received only supportive care and oxygen. In a small series from Johns Hopkins the mortality rate was reduced to 60%

with respiratory support, on average for 18.6 days (104). The radiographic features are presented in Table 26.

Table 26

Radiographic Features of Influenza Pneumonia in 31 Patients

Feature	Percent
Perihilar infiltrates	94
Lobar consolidation	56
Pleural effusion	14
Cavitation	0

Perihilar infiltrates resembling the pulmonary edema pattern of ARDS is reported in all series. In addition, superimposed lobar consolidation resembling aerobic bacterial pneumonia may be present in half of the patients. Small pleural effusions were uncommon, and cavitation was not reported. In the two surviving patients in one series, radiographic clearing occurred at four days and at two months. In the series with five survivors associated with ventilatory support, infiltrates "compatible with pulmonary fibrosis" persisted at one year and were associated with pulmonary function abnormalities which did not limit function.

The drugs listed in Table 27 inhibit Influenza A viral replication but have no activity against influenza B.

Table 27

Prophylaxis and Therapy of Influenza A Infections in the Elderly

Amantadine	≤100 mgm/d
Rimantidine	≤100 mgm/d

Two antiviral agents have been studied in patients with influenza, but only Amantadine hydrochloride is approved by the FDA and presently available for use. Both drugs have been shown to reduce clinical symptoms in elderly persons and shorten the duration of influenza when begun within forty eight hours of onset of symptoms (105). Thus, treatment is recommended if the diagnosis is suspected in the appropriate clinical setting. The total duration of treatment should be five to seven days. Likewise both drugs have been shown to be approximately 70% effective in prophylaxis of Influenza A in elderly patients in nursing homes (106, 107), and the CDC recommends this procedure to prevent or abort nosocomial outbreaks (108). In such instances the staff should also receive the drug.

Persons over 65 have been shown to require half the weight-adjusted dose given to young adults to achieve equivalent plasma levels (109). Dosage of 100 mgm per day should not be exceeded in the elderly, and there is need for further reduction if the renal function is impaired. Side effects are related to the central nervous and gastrointestinal systems. Central nervous system effects are more prominent with Amantadine and include nervousness, insomnia, dizziness, lack of concentration and seizures. These effects are more frequent and severe in the elderly and may require drug discontinuance (106). The incidence of side effects is also increased by concomitant use of antihistamines or anticholinergic drugs (110).

Bacterial pneumonia in association with influenza was well documented in the 1918 influenza pandemic (111-113). An increased incidence of bacterial superinfection has been reported in the elderly (114). Clinical features of this syndrome listed in Table 28 have not been age-related (101, 102, 114, 115).

Table 28

Clinical Features of Bacterial Pneumonia Complicating Influenza in 60 Patients

Feature	Percent
Latent onset >3 days	94
Purulent sputum, hemoptysis	80
Dyspnea, tachypnea, cyanosis	90
Pleuritic chest pain	50
Pleural effusion	30
Cavitation	5
Mortality	25-80

Bacterial pneumonia complicating influenza rarely begins with the onset of the symptoms of influenza. The delay ranges from 3-12 days and most commonly occurs as the patients are recovering from the viral infection. Cough, purulent sputum, hemoptysis, severe dyspnea, tachypnea and cyanosis are similar to influenza viral pneumonia. However, pleuritic chest pain and pleural effusion are significantly more common with bacterial infection. Cavitation when present is highly suggestive of bacterial infection. No other laboratory or radiographic features have proven useful in a differential diagnosis. Mortality has varied from 25-80%, considerably less than influenza viral pneumonia.

Etiologies of bacterial pneumonia apparently vary between epidemics, but each has included Streptococcus pneumoniae, Staphylococcus aureus, Hemophilus influenza and various gram negative bacilli. Among autopsy studies mixed bacterial infection can be demonstrated in up to 50%. Treatment

recommendations are therefore similar to those for aerobic bacterial pneumonia that is nursing home acquired. Vancomycin should be added if methicillin resistant organisms have been reported.

C. Respiratory Syncytial Virus

Respiratory syncytial virus has increasingly been recognized as the etiology of outbreaks of pneumonia in nursing homes (116). This finding is not unexpected, since the virus has been shown to have an increased attack rate in children and in older persons (Table 29) (117).

Table 29

Age Related Evidence of
Respiratory Syncytial Virus Infection

	Age (years)		
	0-19	20-50	50-88
No. pts. tested	276	302	315
No. cases RSV	14	7	18
Percent infected	5	<1	6

Fransen tested all patients admitted with a diagnosis of respiratory illness to The Hospital for Infectious Diseases in Stockholm from the years 1963 to 1966. RSV infection was diagnosed by a greater than four-fold CF antibody titer rise. Infection with RSV in children and older adults was approximately 5 percent of cases, but it rarely occurred between ages 20 and 50. The majority of RSV infections were in children less than age six and persons over the age 70. Additionally, attack rates of RSV infection of approximately 10% in persons over the age of 80 have been reported from two chronic care facilities (116, 118).

Clinical features of serologically documented respiratory syncytial virus infection in the elderly are listed in Table 30 (91, 116-118).

Table 30

Clinical Features of Respiratory
Syncytial Virus Infection in the Elderly

Feature	Percent of Patients			
	Morales n=12	Fransen n=18	Mathur n=7	Sorvillo n=40
Cough	100	100	100	90
Myalgias, malaise	-	80	71	-
Rhinorrhea	20	-	100	90
Fever >38°C	50	89	100	80
Resp. rate >20	100	-	-	-
Wheezing	83	-	-	-
Pneumonia	20	44	42	53
Mortality	33	0	-	20

Cough, myalgias, malaise, rhinorrhea and a temperature of >38° have been reported in the majority of patients. An increased respiratory rate is also apparently a consistent feature. RSV infection in infants and children is frequently associated with bronchiolitis obliterans. In one report wheezing occurred in 83% of aged persons, and there have been several reports of a lower respiratory tract illness lasting up to eight weeks in elderly persons (119, 120). The reported incidence of pneumonia diagnosed by radiographic infiltrates may represent either viral or superimposed bacterial pneumonia similar to the syndromes described in influenza. The 44% of Fransen's patients with radiographic infiltrates apparently all had true RSV pneumonia. The reported mortality following RSV infection in this age group has varied from 0 to 33% (121-123). The largest series by Sorvillo reporting a death rate of 20% may be the most realistic estimate. It is clear from this review that RSV is second to influenza in causing viral pneumonia in the elderly both in the community and in nursing homes and causes more serious disease than in younger adults.

The radiographic features of serologically documented RSV pneumonia are listed in Table 31 (116, 117).

Table 31

Radiographic Features of Respiratory Syncytial Virus Pneumonia in the Elderly

Feature	Percent of Patients Sorvillo n=40	Fransen n=18
Bilateral	60	67
Patchy pneumonitis	45	22
Diffuse consolidation	55	-
Lower lobes	80	-

Radiographic changes are nonspecific and follow the pattern seen in influenzal pneumonia. Infiltrates are most often bilateral, may be patchy or consolidative, and have a propensity for lower lobes. Bilateral, diffuse, nonspecific interstitial infiltrates, such as those seen in ARDS, have also been reported. Recent reports of the efficacious use of inhaled ribavirin in the treatment of life threatening pneumonia should encourage physicians to attempt to make this diagnosis when suggested by the clinical findings (123-127).

Tests available for rapid detection of RSV are listed in Table 32 (128-130).

Table 32

Laboratory Tests for Rapid Detection of Respiratory Syncytial Virus

Immunofluorescence
ELISA
Cytology

Virus isolation remains an investigational technique, and a rise in complement fixing antibodies is not clinically relevant in an acute illness. Immunofluorescence on respiratory cells obtained by nasopharyngeal aspiration detects viral antigen using a bovine anti-RSV serum and a second fluorescein-labeled anti-bovine immunoglobulin reagent. Results using IF are highly sensitive and specific when compared to viral isolation (128). Enzyme-linked immunosorbent assay (ELISA) kits are also available for the detection of antigen in nasopharyngeal aspirates. The sensitivity and specificity of the ELISA is similar to the immunofluorescent technique (129, 130). When infected with RSV respiratory epithelial cells from the nasopharynx or trachea have multinucleated cells and intracytoplasmic basophilic inclusions with prominent halos (131). Cytological diagnosis depends on the skill of the cytologist.

If RSV infection is confirmed, there is clinical evidence that aerosolized ribavirin should be used in seriously ill patients (123-125). Adults on ventilators have apparently been effectively treated with 6 gm of lyophilized ribavirin delivered as an aerosolized solution over a continuous 22 hour period daily for 5 consecutive days (125).

D. Parainfluenza

Parainfluenza virus Types 1, 2, and 3 have also been reported to cause outbreaks of lower respiratory tract infection in nursing home residents. The illness is usually a mild bronchitis, and treatment is not recommended. There is evidence for person to person spread, and isolation of residents during a recognized outbreak is recommended (132).

E. Adenovirus

Adenovirus has also been reported to cause bronchitis in older persons (90). The disease is usually mild and self limited. This virus has not been described as an etiology of pneumonia in a nursing home population.

F. Mycoplasma pneumoniae

Mycoplasma pneumoniae is usually considered only in the differential diagnosis of atypical pneumonia in younger patients. However, this organism has been reported in persons over 60 years in two large series (Table 33) (90, 133).

Table 33

Prevalence of Community Acquired Pneumonia in the Elderly Due to Mycoplasma

	Mufson	Marrie
No. pts. with pneumonia	346	719
No. pts. with M. pneumoniae	16	40
Percent	5	6

These studies were performed on patients hospitalized for pneumonia. The agent was confirmed by a four-fold rise in CF antibody titers to Mycoplasma species. Both studies indicated a prevalence of approximately 5%. Marrie additionally demonstrated that Mycoplasma infection in this age group is essentially limited to community based patients. Less than 1% of patients with pneumonia admitted from nursing homes had Mycoplasma as an etiology. Additionally, several studies have documented a significant attack rate of pneumonia in older family members during an outbreak of Mycoplasma infection in families (134-136). Thus, Mycoplasma pneumonia should be strongly considered in

elderly patients who are community based with significant exposure to younger persons.

Data on clinical features unique to the elderly are not available. Mycoplasma pneumonia in adults was reviewed in a Grand Rounds in 1987 and will not be repeated here (137). It should be noted, however, that a spectrum of disease severity has been reported in older persons ranging from minor symptoms to respiratory failure. Ten percent of older patients with Mycoplasma pneumonia has been reported to require mechanical ventilation (133).

G. Chlamydia pneumoniae (Strain TWAR)

Chlamydia pneumoniae (Strain TWAR) has only recently been established as a important cause of atypical pneumonia in adults, accounting for 6 to 12% of community acquired pneumonia in several series (86, 138). Infection in childhood is common with reinfection occurring throughout adult life (139, 140). Disease in the older age group has been clearly established and may have severe symptoms (141).

The clinical features of Chlamydia pneumoniae in both young and elderly persons are listed in Table 34 (141, 142).

Table 34

Clinical Features of Chlamydia Pneumoniae in the Young and Elderly

Feature	Percent of Patients <25 years	>64 years
Cough	100	61
Headache	57	22
Sore throat	71	-
Hoarseness	14	-
Fever >37.8°	14	56
WBC >10,000/mm^2	15	61
Chronic disease	-	70
Abnormal B.S.	93	89

Typically, Chlamydia pneumoniae in younger patients causes a relatively mild illness presenting with a prominent cough, headache, sore throat, and occasionally hoarseness. Patients may not be febrile, and the WBC is usually not elevated. In contrast older persons usually have serious underlying disease and tend to be febrile with a leukocytosis. Cough and headache are not as prominent, and a major component of sore throat and hoarseness has not been described. The lung exam is abnormal in both groups.

Chlamydia pneumoniae has only been reported in community based elderly patients. However, hospital transmission has occurred in younger patients, and nursing home transmission may well be demonstrated when additional studies are performed.

Protracted cough has been described in all age groups but morbidity and mortality are clearly increased in elderly patients (141, 142). Antibodies to Chlamydia can be found in up to 77% of patients with chronic obstructive lung disease suggesting infection is common in this group.

The radiographic features of Chlamydia pneumoniae are listed in Table 35 and differ in age group (138, 141, 143, 144).

Table 35

Radiographic Features of Chlamydia pneumoniae in the Young and the Elderly

Feature	<25 years	>64 years
One lobe	80	61
Two lobes	5	39
Diffuse	15	5
Pleural effusion	0	30
Lower lobes	60	72

In younger patients Chlamydia pneumoniae is primarily a lobar disease but may be diffuse as seen in viral and mycoplasma infection. Pleural effusions have not been reported, and the lower lobes are primarily involved.

In the elderly up to 40% will have two or more lobes involved and pleural effusions have been reported in up to 30%. Again, lower lobes are primarily involved, but diffuse infiltrates are uncommon.

The diagnosis of Chlamydia is more difficult than that of viral or mycoplasma infection. Cultural isolation is possible only investigationally. Immunofluorescent antibodies to Chlamydia pneumoniae strain TWAR is the only sensitive and specific serologic test available. Serology should be interpreted by the criteria developed at the University of Washington and listed in Table 36 (139).

Table 36

Serologic Tests in Diagnosis of
Chlamydia Pneumoniae Strain TWAR

Micro IF with TWAR antigen	
Acute infection	Four-fold rise in IgM, IgG antibody titer **or** IgM ≥1:16 **or** IgG ≥1:512
Pre-existing infection	IgG ≥1:16 and <1:512
Chlamydia CF (nonspecific)	Four-fold rise ≥1:64

The microimmunofluorescence test can distinguish IgM and IgG antibodies. Acute infection is considered as a four-fold rise of either IgM or IgG antibody or a TWAR specific IgM fractions of ≥1:16 or a TWAR specific IgG fraction of ≥1:512. Past infection is assumed if the TWAR specific IgG fraction is ≥1:16 and less than 1:512.

The chlamydia complement fixation test is nonspecific and detects antibodies to Chlamydia pneumoniae, Chlamydia trachomatis, and Chlamydia psittaci. Acute infection may be diagnosed with either a four-fold antibody titer rise or a initial titer of equal to or greater than 1:64. A four-fold titer rise in the absence of exposure to sick birds is highly suggestive of Chlamydia pneumoniae. The complement fixation test is limited by the fact that it frequently fails to show antibody in reinfection, and most older patients with TWAR disease will fail to demonstrate CF antibody (86, 138, 141).

Timing of collections of specimens for serologic studies is important since the two patterns of antibody response listed in Table 37 have been found (139).

Table 37

Appearance of Antibodies to Chlamydia
(Weeks Following Onset of Infection)

Antibody	First Infection	Reinfection
IgM	2-4	May not appear
IgG	6-8	1-3
CF	2-3	May not appear

Older patients usually have a reinfection pattern, since initial infection frequently occurs in childhood. If infection is clinically suspected, serology should be obtained with the onset of illness and again in 3 to 4 weeks in order to determine maximal IgM and CF antibody response to a first infection and maximal IgG response to a reinfection. If diagnosis remains in question, a third specimen obtained at 6-8 weeks may be helpful.

There have been no controlled studies of antibiotic treatment of Chlamydia pneumoniae infections. Recommendations for treatment are based on the in vitro sensitivities listed in Table 38 (145, 146).

Table 38

In Vitro Antibiotic Sensitivities
of Chlamydia Pneumoniae Strain TWAR

Antibiotic	Minimum Inhibitory Concentration (per ml)
Tetracycline	0.05 - 1.0 μg
Doxicycline	0.25 μg
Erythromycin	0.01 - 0.06 μg
Ciprofloxacin	2.0 μg
Ampicillin	>100 μg
Sulfamethoxazole	>400 μg

Tetracycline, doxicycline and erythromycin are equally effective. The quinalones are less effective and the penicillins and sulfas are clearly ineffective. Tetracycline or erythromycin is given in a dose of 500 mgm four times a day for 14 days. Doxicycline is given at 100 mgm every 12 hours for 14 days. Symptoms, particularly chronic cough, are slow to respond, and treatment may be necessary for up to a month.

VIII. PREVENTION

A. Influenza Vaccine

In recent years influenza vaccine has contained two subtypes of influenza A virus and one subtype of influenza B virus. Antigenic drift of the virus results in new strains and subtypes. New subtypes appear at intervals of 9 to 39 years and are capable of causing pandemics. Antigenic drift within subtypes occurs yearly and results in new strains. The vaccine strains are altered yearly to reflect strains that circulated the previous winter, particularly toward the end of the season (147-148). Influenza vaccination is recommended for nursing home residents and for all persons over the age of 65 years by the Immunization Practices Advisory Committee of the CDC (149).

Antibody response and hence vaccine effectiveness range from 70-90% among healthy young populations (150-151). Studies in elderly patients generally have shown only a moderately good and a variable antibody response compared to young persons (152, 153). A recent review of available literature presented in Table 39 summarizes expected effectiveness in persons over 65 years (98).

Table 39

Efficacy of Influenza Vaccine
in the Elderly

	Percent Reduction	
	Community	Institutionalized
Morbidity	5	33
Mortality	47	74

Several large series were summarized, and effectiveness was calculated as a 33% reduction in morbidity and a 74% reduction in mortality of the institutionalized elderly. In the community based elderly, however, only a significant reduction in mortality could be demonstrated.

Efficacy of influenza vaccination has also been evaluated in the prevention of hospitalization and in severity of illness among both the community based and institutionalized elderly (Table 40) (154, 155).

Table 40

Efficacy of Influenza Vaccine
in the Elderly

	Vaccinated	Unvaccinated
Attack Rate	20%	33%
Hospitalization	2%	63%
Severity of illness score	.24	.36

Attack rates of infection was not significantly different in vaccinated and unvaccinated persons. However, hospitalizations, commonly for pneumonia, were decreased from 63% to 2%, and the severity of illness score was also significantly different. These observations suggest that influenza virus vaccine is more effective in reducing the severity of illness and occurrence of complications than it is in preventing illness in older persons (156-158). Thus, the recommendation to vaccinate all persons over 65 yearly regardless of residency is well supported.

B. Pneumococcal Vaccine

A polyvalent pneumococcal vaccine against 14 of the 83 serotypes of pneumococci was first approved in 1977. This vaccine was replaced in 1983 by a vaccine against the 23 serotypes of the organism that account for 88% of bacteremic pneumococcal disease in the United States (159). Vaccine efficacy is classically measured as the difference in attack rate (AR) for a specific disease between immunized and nonimmunized cohorts as expressed in the following formula:

$$\text{Efficacy} = \frac{\text{AR in unimmunized} - \text{AR in immunized}}{\text{AR in unimmunized}} \times 100$$

There is no question that this vaccine is highly effective in young, immunologically intact persons among populations with a high incidence of pneumococcal disease (160, 161). Efficacy in the elderly has been more difficult to determine. Results of several studies performed in older persons are presented in Table 41 and have yielded conflicting results (162-167).

Table 41

Efficacy of Pneumococcal Vaccine in the Elderly

Study	Mean Age	No.	% Efficacy
Sims, Shapiro	66	909	60-70
Simberkoff, Forrester	65	2473	0
Bolan, Gaillat	65	5340	44-70

Sims and Shapiro reported community based elderly patients and excluded those in the highest risk groups. Each reported the vaccine to be efficacious in healthy older patients that were presumed to be immunocompetent. Both Simberkoff and Forrester were unable to demonstrate efficacy of pneumococcal vaccine. Each study included large numbers of patients who did not demonstrate an adequate immune response to the vaccine. Simberkoff was able to correlate poor immunologic response with vaccine failure. Bolan's study from the CDC included persons residing in nursing homes with chronic heart disease, pulmonary disease and diabetes mellitus as well as those in lower risk groups. Overall efficacy was found to be 44%. Gaillat in a study from France where the attack rate of pneumococcal disease is higher than in the United States found an efficacy of 70%. The study was large, prospective and randomized. Patients in highest risk groups were excluded.

I infer from these data that efficacy of pneumococcal vaccine is inversely related to degree of chronic illness and to immunoincompetence. However, I agree with others that vaccination should be recommended for all persons over 55 years with an increased emphasis on those who are healthy. Efficacy of vaccination in debilitated patients with chronic disease is questionable (167).

Studies on revaccination have also conflicted. Several investigators have demonstrated an increase in local reaction which may be severe (168-170). The current recommendation is to not revaccinate persons who received the 14 valent vaccine with the 23 valent vaccine (159). However, there is increasing evidence that clinical efficacy may decline after 6 years, and revaccination is currently recommended for patients with the nephrotic syndrome, renal failure or transplant recipients (159). This recommendation is likely to be extended to other high risk elderly in the near future.

SUMMARY

As first noted by Osler pneumonia remains "a special friend of old age". An increase in nursing home residence has changed the identity of the friend but the friendship remains intact. Along the way new friends have also been acquired. Caring for the elderly necessitates a knowledge of all these relationships.

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