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for unwanted substances (such as excess fluid in pulmonary edema) in the lung parenchyma, it is unlikely that the pleural space exists solely for such purpose.

Studies on pleurodesis, the iatrogenic obliteration of the pleural space to prevent recurrent effusions or pneumothoraces, showed no significant limitations to pulmonary functions. Patients who received talc pleurodesis over 22 years ago for spontaneous pneumothoraces showed a higher incidence of pleural thickening but minimal restrictive changes in lung functions. Several small studies in humans and animals also revealed no significant impairment in lung volumes and gaseous exchange at rest or during exercise following pleurodesis.

The fact that obliteration of the pleural space does not affect health and functioning supports the belief that the pleural space in humans serves no significant role. Why the pleural space exists in the first place and why it is preserved through evolution remain unanswered.

See also: Mesothelial Cells. Mesothelioma, Malignant. Pleural Effusions: Overview; Pleural Fluid, Transudate and Exudate; Pleural Fluid Analysis, Thoracentesis, Biopsy, and Chest Tube; Parapneumonic Effusion and Empyema; Malignant Pleural Effusions; Postsurgical Effusions; Pleural Fibrosis; Chylothorax, Pseudochylothorax, LAM, and Yellow Nail Syndrome; Hemothorax. Pneumothorax.

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types of pneumonia always includes the common community-acquired pathogens, with the spectrum broadening in response to either increasing immunocompromise or greater exposure to broad-spectrum antibiotics. While new or previously unrecognized pathogens can play a role in management decisions, the major issue in pneumonia is the appearance of antibiotic resistant strains of known common bacterial pathogens. Lack of even minimally effective agents is more the issue for nonbacterial pneumonias. Immunomodulation, in the form of less immunosuppressive cancer and transplant chemotherapy, immunization, or specific immunomodulatory drugs holds some hope for improving pneumonia outcome in the future.

Definitions

Pneumonia is the infection of the distal lower respiratory tract, principally the alveolar space, including the small bronchi and bronchioles. Pneumonia results from the proliferation of microorganisms at these sites in combination with the host response to the presence of microorganisms. Proliferation alone does not necessarily result in pneumonia, since many patients on chronic mechanical ventilation will have quantitative colony counts thought to be diagnostic of pneumonia in other settings without any clinical manifestations of pneumonia. Presence of microorganisms without a corresponding host immune reaction is designated as colonization.

Infection at the alveolar level distinguishes pneumonia from other respiratory tract infections with which it may be confused clinically. Infections of the conducting airways below the vocal cords are designated as tracheitis, bronchitis, or bronchiolitis, depending on the main area of involvement. These are at times combined as lower respiratory tract infections (LRTIs) to distinguish them from upper respiratory infections (URIs). The latter, which include laryngitis, pharyngitis, and rhinitis, are generally more common, more often viral, and generally less serious. Diphtheria, acute epiglottitis, and pertussis are some of the exceptions to these general rules that suggest careful distinction and accurate diagnosis are critical to clinical care.

Even within the designation of pneumonia a variety of pneumonia syndromes occur (Table 1). These can be classified in a number of ways based on microbial etiology, underlying host defenses, and clinical presentation, among others. The most common initial grouping is by patient location at time of acquisition, that is, community-acquired or nosocomial pneumonia. Recently, a third category has been added: healthcare-associated pneumonia (HCAP) (Table 2). This category was needed to designate patients with pneumonia developing outside the hospital but whose pathogenesis, causative agents, and antibiotic resistance patterns were more consistent with nosocomial pathogens. The majority of these patients are from nursing homes but the group also includes chronic dialysis patients or others with frequent or recent contact with the medical system. Within each of these categories, patients with compromised immunity are usually discussed separately, since the spectrum of causative etiologies is much larger and therefore the diagnostic and therapeutic approaches differ from that of patients with overtly normal host immunity. Most of these pneumonia syndromes have separate entries in this encyclopedia.

Pathology

The common component to the pathology of pneumonia is an inflammatory response within the lung parenchyma. The pattern of inflammatory response will vary by causative etiology. Mycobacterial and fungal infections result in a granulomatous response characterized by histiocytes and mononuclear cell proliferation. Most bacterial pneumonias result in a neutrophilic alveolitis while many viruses and obligate intracellular agents generate a lymphocytic alveolitis.

The key to the development and pattern of pneumonia is the alveolar macrophage. The overwhelming

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**Table 1** Pneumonia syndromes

| Category | Description |
|----------|-------------|
| 1. Community-acquired pneumonia | a. Typical (normal host) i. Bacterial ii. Viral iii. Fungal iv. Mycobacterial v. Parasitic/other b. Immunocompromised i. Acquired immunodeficiency syndrome ii. Other c. Aspiration pneumonitis/lung abscess |
| 2. Healthcare-associated pneumonia (HCAP) | a. Nursing home pneumonia b. Other |
| 3. Nosocomial pneumonia a. Ventilator-associated b. Immunocompromised i. Transplant-related ii. Chemotherapy-related |

**Table 2** Healthcare-associated pneumonia

| Criteria |
|----------|
| Antibiotic therapy in the preceding 3 months |
| Hospitalization for at least 2 days in the preceding 90 days |
| Residence in a nursing home or extended care facility |
| Home infusion therapy (including antibiotics) |
| Chronic dialysis within 30 days |
| Home wound care |
| Immunocompromised state (disease or immunosuppressive therapy) |
majority of microorganisms that reach the alveolar level are killed and/or cleared by the alveolar macrophage without inducing an inflammatory response. Simply to get to the alveolar level means that the microorganism has avoided all the mechanical and other host defense mechanisms of the upper respiratory tract and the conducting airways. These include the branching airway pattern and the mucociliary clearance mechanisms, mucosal immunoglobulins, complement, surfactant, lactoferrin, defensins, and other antimicrobial peptides. Given the microbial particle challenge presented to the respiratory tract on a daily basis, these mechanisms are highly efficient at preventing an overwhelming challenge to the alveolar macrophage.

However, either because of the virulence or the volume of microorganisms that it is exposed to, the alveolar macrophage can be overwhelmed. The response is release of a variety of mediators that elicit an inflammatory response appropriate for the particular challenge. The inflammatory response, rather than sheer numbers of microorganisms, is responsible for the radiographic changes of pneumonia while the mediators released as part of the inflammatory response result in many of the clinical manifestations, such as fever and leukocytosis.

Microorganisms can reach the alveolar level through two major mechanisms: aerosol deposition and aspiration of an infected bolus. The former is the mechanism for most viral, mycobacterial, and fungal infections while many of the bacterial pneumonias are a result of aspiration. Aspiration pneumonia is a specific variant of aspiration pneumonia that is characteristically polymicrobial with prominent involvement of anaerobic bacteria. In this disorder, a large volume aspiration episode, usually from a seizure or alcoholic stupor, occurs days to weeks before presentation with the signs and symptoms of pneumonia. The aspirated bolus is usually enriched with anaerobic microorganisms by the presence of severe gingivitis, which explains the fact that this syndrome is very rare in the edentulous. The presence of anaerobes often results in a lung abscess and corresponding severe pleural reaction.

Only rarely do two other mechanisms allow microorganisms to appear at the alveolar level. The first is hematogenous spread. While this clearly can occur with tricuspid endocarditis, the bronchocentric (rather than vasocentric) pathology of most bacterial pneumonias suggests that this is rare even in immunocompromised patients with other sites of infection. The second mechanism is direct spread from a contiguous site of infection, such as infradiaphragmatic infections or primary empyema.

The mechanism by which microorganisms reach the lower respiratory tract has important implications for prevention and infection control.

**Diagnosis**

The diagnosis of pneumonia rests disproportionately on the presence of an infiltrate on chest radiograph. Pneumonia should be considered in any patient who has newly acquired respiratory symptoms (cough, sputum production, dyspnea, and chest pain), especially if accompanied by fever and auscultatory findings of abnormal breath sounds, particularly crackles. In the elderly and those with an inadequate immune response, pneumonia may present with nonrespiratory symptoms such as delirium, fatigue, failure to thrive, worsening of an underlying chronic illness, or a fall. In elderly patients, fever may be absent but tachypnea is usually present, along with an abnormal physical examination of the chest. Unfortunately, none of these symptoms is unique to pneumonia. Many of both symptoms and clinical signs can occur with other LRTIs. Hence the dependence on an abnormal chest radiograph for an accurate diagnosis.

Unfortunately, the plain chest radiograph is not a reliable standard on which to base a diagnosis. Significant inter- and intraobserver variability exists in interpretation. The problem is particularly acute in patients suspected of ventilator-associated pneumonia (VAP) where not only multiple radiographic mimics of pneumonia exist but also simply changing ventilator settings will alter the radiograph. In patients with underlying pulmonary disease, differentiation between an infectious process and the deterioration of the underlying pulmonary disease is also often difficult.

Occasionally, patients with pneumonia may have chest radiographs interpreted as normal. Most of these false-negative readings represent subtle findings overlooked in a routine interpretation. Interpretation can be improved by obtaining a standard upright posteroanterior (PA) and lateral views whenever possible. Use of more sensitive techniques, such as computed tomography (CT), can often detect these infiltrates. Occasionally, severe dehydration or lack of circulating neutrophils will prevent the radiographic changes of pneumonia until the underlying deficit is corrected.

Despite its shortcomings, the radiograph can be useful in differentiating pneumonia from other conditions that may clinically mimic it. Moreover, the radiographic findings may suggest specific etiologies or conditions, including lung abscess or tuberculosis. The radiograph can also identify coexisting...
conditions, such as bronchial obstruction or pleural effusion, and may be helpful in evaluation of the severity of illness by identifying multilobar involvement.

The diagnosis of pneumonia is actually a two-step process. The first is determining that pneumonia is indeed present. However, for optimal antimicrobial management an etiologic diagnosis is also needed. Demonstrating the presence of a microorganism in culture or in stains of pathologic specimens are the classic methods to demonstrate the causative agent. Once again these methods are woefully inadequate for diagnosing pneumonia. The reason varies depending on the type of pneumonia. In community-acquired pneumonia (CAP), many of the causative microorganisms are not easily grown in culture and even with the most aggressive culture and extensive use of other diagnostic modalities, the etiologic diagnosis remains unknown in the majority of cases. In contrast, for nosocomial pneumonia, especially VAP, the high incidence of colonization frequently results in many false-positive cultures and polymicrobial cultures in monomicrobial pneumonias. For some of the chronic pneumonias such as tuberculosis and endemic fungal disease, the slow growth characteristics delay a definitive microbiologic diagnosis for weeks. The net result is that the antimicrobial treatment of pneumonia is often empiric. Clearly, new nonculture-based diagnostic methods are needed.

This lack of a microbiologic diagnosis and the non-specificity of signs, symptoms, and radiographic infiltrates leads to frequent consideration of pneumonia in the differential diagnosis of many pulmonary diseases. Essentially any disorder that can cause signs or symptoms of inflammation and an abnormal radiographic infiltrate can be mistaken for pneumonia. The differential diagnosis varies somewhat among the various CAP syndromes. Table 3 lists many of the entities in the differential diagnosis but is by no means exhaustive.

The differential diagnosis expands further if prior radiographs and clinical information is not known. Bronchitis or even URIs can be mistaken for pneumonia in patients with previously unknown chronic infiltrates. Common combinations of disorders can also mimic pneumonia. For example, congestive heart failure can often be complicated by influenza. If the patient also has chronic obstructive pulmonary disease (COPD), asymmetric infiltrates may be seen. This problem is worst in patients with suspected VAP because of the poor radiographic technique and multiple other causes for fever or leukocytosis in the critically ill.

Presence of pneumonia and a putative etiology is often assumed by an ‘appropriate’ response to antibiotics. However, many of the diseases in the differential may be self-limiting or respond to adjuvant therapy for pneumonia and therefore falsely suggest that the diagnosis is pneumonia. Conversely, 15% of CAP patients and up to 40–50% of cases of VAP due to specific etiologies do not respond even to specific therapy.

### Epidemiology

Pneumonia remains a common and serious illness despite the availability of potent antimicrobials and effective vaccines. In the US, pneumonia is the seventh leading cause of death and the number one cause of death from infection. A similar annual rate of approximately 50–60 cases per 100,000 is probably the case in most developed countries. However, data regarding its incidence are suboptimal because pneumonia is not a notifiable disease. The US data

| Community-acquired | Nosocomial |
|--------------------|------------|
| Pulmonary embolus/infarction | Atelectasis |
| Congestive heart failure | Atypical pulmonary edema |
| Malignancy | Acute respiratory distress syndrome (ARDS)/diffuse alveolar damage |
| Bronchogenic with airway obstruction | Aspiration pneumonitis |
| Bronchoalveolar cell | Lung contusion |
| Acute respiratory distress syndrome (ARDS) – nonpulmonary source | Drug-induced lung disease |
| Drug-induced lung disease | Pleural effusion |
| Radiation pneumonitis | Pulmonary hemorrhage |
| Vasculitis | Pulmonary infarction |
| Systemic lupus erythematosis | Bronchiolitis obliterans with organizing pneumonia (BOOP) |
| Wegener’s granulomatosis | Acute transplant rejection |
| Hypersensitivity pneumonitis | |
Community-Acquired Pneumonia

The overall incidence of cases of CAP is approximately 10–12 per 1000 persons per year; however, this varies considerably with age, sex, race, and socioeconomic condition. The incidence of CAP is highest among the oldest and youngest members of the population. In the US, the highest incidence is in children younger than 4 years of age (12–18 cases per 1000 persons per year), which is similar to the rate reported in older individuals (age ≥ 60) in Europe (20 cases per 1000 persons per year). Pneumonia accounts for nearly half of all deaths resulting from infectious disease in the geriatric population, and 90% of all deaths from respiratory tract infection occur in persons older than 64 years. However, while the case fatality rates are increased in both the very young and the elderly, more than 50% of deaths from pneumococcal pneumonia occur in patients aged 18–65 years.

Approximately 4 million cases of CAP are estimated to occur annually in the US, resulting in 600,000 hospitalizations per year. Despite its frequency, pneumonia is the cause of acute LRTI symptoms in only a small minority of patients from the community. In one prospective study of LRTIs requiring antibiotics in adults seeking attention from a physician, only 12% of patients were found to have pneumonia.

The majority (up to 80%) of patients with CAP are treated as an outpatient with a mortality rate of less than 1% in these patients. The need for hospitalization varies widely depending on characteristics of the healthcare system and physician preference. The incidence has ranged from 15% to 42% in both European and North American studies. The frequency of admission of patients at low risk of death by various prediction models varies greatly and physicians in general overestimate the risk of dying from CAP. Among patients who have pneumonia of sufficient severity to require admission to hospital, reported mortality rates range from 4% to as high as 37% and increase with increasing age. Generally, the higher mortality rates are found in the US where greater use of outpatient treatment and more aggressive treatment of terminally ill patients results in an overall sicker population of patients admitted for CAP.

Admission to an intensive care unit (ICU) also varies dramatically by country and individual hospital. Generally, a higher percent of patients with CAP are admitted to the ICU in North America (>15%) than in Europe (5–10%). In hospitals or areas with limited ICU resources/beds, a much higher number of CAP patients admitted to the ICU have either vasoressor-dependent septic shock or respiratory failure. The associated mortality is inversely proportional to the number admitted, mainly because the mortality in ventilated or septic shock patients is much greater. Mortality is as high as 50% in ICUs where nearly all patients are ventilated, while mortality decreases to 20–30% in ICUs where less than half of patients with severe CAP are ventilated.

Healthcare-Associated Pneumonia

Defining HCAP as a new entity has complicated the epidemiology of CAP, since studies that did not
distinguish this subgroup would have classified these patients as CAP. While clearly recognized as being distinct from usual CAP, no extensive study of HCAP has been published. The majority of HCAP patients are from nursing homes or other chronic care facilities and a few epidemiologic studies have focused on this group of pneumonia patients. Whether other types of HCAP, for example, in patients receiving long-term home parenteral antibiotics or chronic hemodialysis patients, have a similar epidemiology to nursing home patients is unclear.

Nursing home-acquired pneumonia (HAP) is the most common form of HCAP. Pneumonia has the highest mortality rate for any nursing home-acquired infection and frequently results in the transfer of cases to the hospital for management. The overall incidence of nursing home-acquired pneumonia varies from 0.3 to 2.5 episodes per 1000 days of resident care.

**Nosocomial Pneumonia**

Nosocomial pneumonia includes both hospital-acquired and ventilator-associated pneumonias. Hospital-acquired pneumonia is defined as pneumonia that occurs at least 48 h after admission to hospital and VAP is defined as pneumonia that occurs more than 48 h after intubation.

Hospital-acquired pneumonia occurs in about 5–10 per 1000 hospitalized patients and complicates the course of as many as 20% of patients undergoing surgery. The incidence is significantly higher in patients undergoing mechanical ventilation, occurring in 10–25% of these patients. Crude rates for VAP range from 1% to 3% per day of intubation and mechanical ventilation. The cumulative incidence increases at this rate for approximately 3–4 weeks then plateaus, such that patients undergoing long-term mechanical ventilation have substantially lower daily attack rates.

Among nosocomial infections, pneumonia has the highest morbidity and mortality. Mortality in such patients is high, being estimated at 30–70% in different series. Only one third to one half of HAP deaths are thought to be due to the infection itself, the remainder of deaths being the result of comorbid disease. By contrast, in the setting of VAP, attributable mortality of VAP is on average lower, being only 27–33% in some studies. In fact, some authors have estimated that the development of VAP may not increase mortality at all after correction for confounding factors that independently influence mortality. While the attributable mortality of VAP may be debatable, development of VAP consistently increases length of stay in survivors by an average of 7–9 days per patient.

**Other Pneumonia Syndromes**

The epidemiology of other types of pneumonia is not as well defined. Pneumonia in the immunocompromised patient is dependent on the type of immunocompromise. Epidemiologic cues for other less common forms of CAP are listed in Table 4. Further information on the epidemiology of these types of pneumonia and specific microorganisms can be found elsewhere in this encyclopedia.

**Etiology**

The etiology of pneumonia depends on several factors including patient’s immune status (i.e., immunocompetent vs. immunocompromised), recent antibiotic use, and location of the patient when pneumonia

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**Table 4** Conditions related to specific pathogens in patients with CAP

| Condition                          | Commonly encountered pathogens                                      |
|-----------------------------------|---------------------------------------------------------------------|
| Alcoholism                        | *Streptococcus pneumoniae* (+ DRSP), anaerobes, Gram-negative bacilli, tuberculosis |
| COPD/smoker                       | *Streptococcus pneumoniae, Hemophilus pneumoniae, Branhamella catarrhalis, Legionella spp.* |
| Poor dental hygiene               | Anaerobes                                                          |
| Exposure to bats                  | *Histoplasma capsulatum*                                           |
| Exposure to birds                 | *Chlamydia psittaci, Histoplasma capsulatum, Cryptococcus neoformans, Influenza* |
| Exposure to rabbits               | *Francisella tularensis*                                           |
| Travel to Southwest US            | *Coccidioidomycosis, Yersinia pestis*                              |
| Travel to Mexico and South America| *Paracoccidiomycoses*                                              |
| Travel to Southeast Asia          | *Burkholderia pseudomallei*                                        |
| Exposure to farm animals or cats  | *Coxiella burnetti* (Q fever)                                      |
| Suspected large-volume aspiration | Anaerobes                                                          |
| Injection drug use                | *Staphylococcus aureus, anaerobes, tuberculosis, Pneumocystis carinii* |
| Recent antibiotic therapy         | DRSP, *Pseudomonas aeruginosa*                                     |

Check in CAP guidelines.

DRSP, drug-resistant *S. pneumoniae*. 


occurred (community acquired vs. nosocomial) (Table 5). However, the causative spectrum always includes the pathogens most frequently associated with acute CAP. VAP in patients recently admitted to the hospital and not receiving antibiotics will mimic the spectrum of acute CAP. Many pneumonias in immunocompromised patients are also caused by the typical CAP pathogens. Two factors combine to shift the spectrum away from that of typical CAP: (1) worsening immunocompromise; and (2) exposure to broad-spectrum antibiotic therapy, especially when prolonged. An example of the former is human immunodeficiency virus (HIV) disease. When helper T-lymphocyte (cluster determinant or CD4) are > 500 cells/mm\(^3\), usual CAP pathogens and tuberculosis are common causes of pneumonia. Once the CD4 count falls below 200 cells/mm\(^3\), opportunistic infections including *Pneumocystis jirovecii* and CMV become more common. Exposure to broad-spectrum antibiotics is enough to shift the spectrum of HCAP toward that of nosocomial pneumonias.

The etiologic spectrum of pneumonia continues to slowly expand. Roughly every decade a new pathogen is added to the spectrum. Most of these newly recognized pathogens are a result of either a change in host immunity, such as the HIV epidemic or bone marrow/stem cell transplants, or improved diagnostic testing. The latter advance in medical practice often provides an explanation for previously enigmatic cases of pneumonia.

Many of these new pathogens are first recognized in conjunction with epidemics. The classic example is legionnaire’s disease. After the initial well-publicized epidemic led to identification of the genus, multiple species were subsequently defined and testing of samples from prior epidemics and random cases retrospectively demonstrated the importance of *Legionella* spp. for pneumonia. Hantavirus pulmonary syndrome was recognized approximately a decade later.

The latest example is the severe acute respiratory syndrome (SARS) epidemic, which first appeared in southeastern Asia in late 2002. The SARS pathogen was subsequently identified as a coronavirus by the World Health Organization (WHO) laboratory network in April 2003. The SARS coronavirus (SARS-CoV) is only distantly related to previously sequenced coronaviruses and is not believed to have circulated in humans previously. SARS-CoV is postulated to be a previously unknown animal coronavirus that mutated and developed the ability to infect humans. The high transmission rates, especially in healthcare settings and households, suggest that little native immunity to this virus existed previously.

### Treatment

While new or previously unrecognized pathogens can play a role in management decisions, the major issue in pneumonia is the appearance of antibiotic resistant strains of known common bacterial pathogens. The emergence of antibiotic-resistant isolates has truly reached epidemic proportions for CAP and VAP. Multidrug-resistant pathogens are the norm for VAP. The emergence of drug-resistant *Streptococcus pneumoniae* (DRSP) is an increasingly common problem worldwide, with more than 40% of all pneumococci in some areas falling into this category by current definitions. Controversy exists, however, about the clinical relevance of *in vitro* resistance in the absence of meningitis, and whether new therapeutic approaches are required and whether resistance influences the outcome of CAP. When resistance to penicillin is present, there is often *in vitro* resistance to other agents. Methicillin-resistant *Staphyloccocal aureus*, previously thought to be exclusively a

### Table 5: Common etiologies for pneumonia

| Community-acquired pneumonia (acute) | Community-acquired pneumonia (subacute) |
|--------------------------------------|-----------------------------------------|
| *Streptococcus pneumoniae* | *Mycobacteria tuberculosis* |
| *Legionella* spp. | *Histoplasmosis* |
| *Helophillus pneumoniae* | *Blastomycoses* |
| *Chlamyphilia pneumoniae* | *Coccidiomycoses* |
| *Staphylococcus aureus* | |
| *Mycoplasma pneumoniae* | |
| *Klebsiella pneumoniae* | |
| *Influenza* | |
| *Respiratory syncytial virus* | |

| Nosocomial pneumonia (all acute CAP organisms plus) | Immunocompromised (all CAP and nosocomial plus) |
|---------------------------------------------------|---------------------------------------------|
| *Pseudomonas aeruginosa* | *Pneumocystis jiroveci (carinii)* |
| Acinetobacter spp. | Cystomegalovirus |
| Enterobacteriaceae | Herpes virus |
|                        | Varicella |
|                        | *Aspergillus* spp. |
|                        | Other fungi |
|                        | *Nocardia* asteroids |

| Healthcare-associated pneumonia (HCAP) | All of CAP and HAP |
|---------------------------------------|-------------------|
|                                      |                   |

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HAP pathogen, is now making an appearance as a cause of CAP.

The common denominator in development of antibiotic resistance is antibiotic over usage. Unfortunately, development of new antimicrobials is slowing and so far has only been successful in fighting a rearguard action against the advance of antibiotic resistance. Some benefit accrues from shortening the course of appropriate antibiotic use, such as for suspected VAP or with surgical prophylaxis. However, avoiding even starting antibiotics for nonbacterial infections, such as outpatient viral URIs, is the strategy most likely to slow this trend.

In contrast to bacterial and a few other types of pneumonia (tuberculous, P. jiroveci), the lack of even minimally effective agents is more the issue for nonbacterial pneumonias. For Aspergillus, non-tuberculous mycobacteria, respiratory syncytial virus (RSV), CMV, SARS, and many other viral agents, cure of pneumonia really depends on reconstitution of the patient's immune system. Clearly more research is needed in this area.

Given the resistance issues with antibiotics and lack of effective treatment for some types of pneumonia, immunomodulatory treatment is an increasingly important consideration for treatment of pneumonia. Immune modulation can take three pathways. One is the development and use of less immunosuppressive treatments for malignancies and transplant patients. Important advances in this area have already resulted in renal transplant patients returning to a near normal response to bacterial pneumonia and infrequent occurrence of opportunistic pathogens causing pneumonia. The second route is immunization. Childhood immunization has a long track record of effectively preventing respiratory infections with pertussis and diphtheria. The only infections seen with these pathogens in developed societies are when vaccination has not been provided. Recently, the use of the Haemophilus influenzae and protein conjugate pneumococcal vaccines have nearly eliminated meningitis from these bacteria and significantly reduced the incidence of respiratory tract infections. Not only has the conjugate pneumococcal vaccine decreased infection in children but it has also resulted in a decrease in invasive infections in the child's adult caregivers. Even the polysaccharide pneumococcal vaccine appears to decrease the rate of invasive disease, even if it does not decrease overall pneumonia rates. The third immunomodulatory strategy is specific immunomodulation for established infection. The use of the colony-stimulating factors filgrastim and sargramostim for neutropenic patients is one example. The recent release of drotrecogin alfa activated (activated protein C) for severe sepsis offers some hope to improve the mortality of bacterial CAP, especially pneumococcal CAP.

Conclusion

Pneumonia is both a common and a significant problem in clinical medicine. While certain aspects of pathogenesis and management are common to all forms of pneumonia, significant differences also exist. These differences are discussed further in other articles specific to the different pneumonia syndromes, pathogens, molecules involved in host immunity, and diseases in the differential diagnosis.

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See also: Antiviral Agents. Atelectasis. Bronchiectasis. Bronchiolitis. Coagulation Cascade; Protein C and Protein S. Colony Stimulating Factors. Defensins. Drug-Induced Pulmonary Disease. Granulomatosis; Wegener's Disease. Human Immunodeficiency Virus. Immunoglobulins. Interstitial Lung Disease; Cryptogenic Organizing Pneumonia; Hypersensitivity Pneumonitis. Laryngitis and Pharyngitis. Leukocytes; Neutrophils; Pulmonary Macrophages. Lung Abscess. Pleural Effusions; Parapneumonic Effusion and Empyema. Pneumonia; Atypical; Community Acquired Pneumonia, Bacterial and Other Common Pathogens; Fungal (Including Pathogens); Nosocomial; Parasitic; Mycobacterial; Viral; The Immunocompromised Host. Pulmonary Thromboembolism; Pulmonary Emboli and Pulmonary Infarcts. Radiation-Induced Pulmonary Disease. Surgery; Transplantation. Systemic Disease; Diffuse Alveolar Hemorrhage and Goodpasture's Syndrome; Eosinophilic Lung Diseases. Tumors, Malignant: Bronchogenic Carcinoma; Chemotherapeutic Agents. Upper Respiratory Tract Infection. Vaccinations; Bacterial, for Pneumonia; Viral. Vasculitis: Overview. Ventilation, Mechanical; Ventilator-Associated Pneumonia. Viruses of the Lung.

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Relevant Website

www.brit-thoracic.org.uk – The British Thoracic Society is formed by the amalgamation of British Thoracic Association and Thoracic Society. It includes medical practitioners, nurses, scientists, and any professional with an interest in respiratory disease.

Atypical

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Abstract

‘Atypical pneumonia’ refers to a clinical syndrome associated with pneumonia (typically mild, nonlobar) and diverse upper respiratory tract and extrapulmonary manifestations. Clinical features overlap with bacterial pneumonia, and co-infection with both typical (e.g., Streptococcus pneumoniae or other bacteria) and atypical pathogens may occur. ‘Atypical’ pathogens include Mycoplasma pneumoniae, Chlamydia pneumoniae, and Legionella spp. In large epidemiological studies, Mycoplasma pneumoniae has been implicated in 2–18% of community-acquired pneumonias; Chlamydia pneumoniae, in 2–8%; Legionella sp., 1–4%. Atypical pathogens lack cell walls and are resistant to β-lactam antibiotics but are usually susceptible to tetracyclines, macrolides, ketolides, and fluoroquinolone antibiotics. In this article, we also review other unusual causes of pneumonia which are transmitted by insects or vectors (e.g., Rocky Mountain spotted fever, cat scratch fever, Q fever, ehrlichiosis, Lyme disease, and tularemia). These diverse organisms are not found on Gram stain, and diagnosis requires special culture techniques or serological assays. We review the salient clinical and laboratory features of these various disorders, and discuss diagnostic and therapeutic strategies.

Introduction

In 1938, Hobart Reimann described a group of patients with an initial mild respiratory illness, often accompanied by headache and sore throat, progressing to pneumonia without sputum production. Because this was a picture very different from the well-known presentation of acute pneumococcal pneumonia, Reimann coined the term ‘atypical pneumonia’ to describe these cases. His observation was confirmed by subsequent similar reports and it was noted that the etiologic agents for these illnesses were unidentifiable on Gram stain and not recovered by culture methods used at the time.

The evolution of diagnostic techniques eventually led to the identification of many of the causative pathogens of atypical pneumonia, including the most significant ones, Mycoplasma, Chlamydia, and Legionella. Clinical features of atypical and typical community-acquired pneumonia (CAP) overlap, and the etiology of CAP cannot be determined on demographic, clinical, or radiologic features. However, the term ‘atypical pneumonia’ remains a useful one and describes a clinical picture characterized by more pronounced systemic than respiratory symptoms, bilateral patchy or interstitial infiltrates on chest radiographs, and negative results on sputum Gram stain and not recovered by culture methods used at the time.

Atypical pathogens are being isolated with increasing frequency in CAP and may occur as co-infecting organisms with typical bacterial pathogens. Recent expert consensus statements recommend that empirical therapy for CAP should include coverage for atypical pathogens. In this article, we discuss many of the important microbes that cause atypical pneumonia, including epidemiology, clinical presentation, and therapy (see Table 1). Additional pathogens that can induce an ‘atypical pneumonia’ picture include viruses (e.g., influenza, adenovirus,