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Community Acquired Pneumonia

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Abstract

Community-acquired pneumonia (CAP) is typically caused by an infection but there are a number of other causes. The most common type of infectious agents is bacteria such as *Streptococcus pneumonia*. CAP is defined as an acute infection of the pulmonary parenchyma in a patient who has acquired the infection in the community. CAP remains a common and potentially serious illness. It is associated with considerable morbidity, mortality and treatment cost, particularly in elderly patients. CAP causes problems like difficulty in breathing, fever, chest pains, and cough. Definitive clinical diagnosis should be based on X-ray finding and culture of lung aspirates. The chest radiograph is considered the" gold standard" for the diagnosis of pneumonia but cannot differentiate bacterial from non bacterial pneumonia. Diagnosis depends on isolation of the infective organism from sputum and blood. Knowledge of predominant microbial patterns in CAP constitutes the basis for initial decisions about empirical antimicrobial treatment.

Keywords

Pneumonia, Community acquired pneumonia, Causative agents, Clinical features, Diagnosis, Antibiotics, Prevention

Introduction

Pneumonia is defined as an acute respiratory illness associated with recently developed radiological pulmonary shadowing which may be segmental, lobar or mutilobar [1]. It occurs about five times more frequently in the developing world than the developed world [2]. The incidence of community acquired pneumonia (CAP) range from 4 million to 5 million cases per year, with 25% requiring hospitalization [3]. The problem is much greater in the developing countries where pneumonia is the most common cause of hospital attendance in adults. Pneumonia are usually classified as community acquired pneumonia, hospital acquired pneumonia or those occurring in immunocompromised host or patient with underlying damaged lung including suppurative and aspiration pneumonia [1].

The Disease

Community acquired pneumonia is commonly defined as an acute infection of the pulmonary parenchyma that is associated with at least some symptoms of acute infection and is accompanied by the presence of an acute infiltrate on a chest radiograph or auscultatory findings consistent with pneumonia (such as altered breath sounds and/or localized rales) and occurs in a patient who is not hospitalized or residing in a long term care facility for > 14 days before the onset of symptoms [4]. Diagnosis depends on isolation of the infective organism from sputum and blood. Knowledge of predominant microbial patterns in CAP constitutes the basis for initial decisions about empirical antimicrobial treatment [5].

Microbial Pathogens

Strep. pneumoniae accounted for over 80 percent of cases of community-acquired pneumonia in the era before penicillin [6]. *Strep. pneumoniae* is still the single most common defined pathogen in nearly all studies of hospitalized adults with community-acquired pneumonia [7-9]. Other bacteria commonly encountered in cultures of expectorated sputum are *Haem. influenzae, Staph. aureus,* and gram-negative bacilli [10]. Less common agents are *Moraxella catarrhalis, Strep. pyogenes,* and *Neisseria* meningitides [11]. Anaerobic bacteria are the dominant pathogens in patients with aspiration pneumonia, lung abscess, or empyema. Transtracheal-aspiration fluid indicated that pneumonitis due to anaerobes cannot be distinguished clinically from other common forms of bacterial pneumonia. The implications are that anaerobes probably account for a substantial number of enigmatic pneumonias and that the diagnostic techniques now in common use cannot detect them [12,13].

Legionella, *Mycop. pneumoniae,* and *Chl. Pneumonia* referred to as the "atypical agents," collectively account for 10 to 20 percent of all cases of pneumonia. All show great variations in frequency according to the patient's age and to temporal and geographic patterns. *Legionella* is reported in 1 to 5 percent of hospitalized adults with community-acquired pneumonia but geographic variation is substantial and detection is problematic. Culture is probably the best method, but a survey showed that 32 percent were unable to grow legionella even from pure cultures, measurement of antigenuria is sensitive and easy, but it is limited to *L. pneumophila* serogroup 1 (70 to 90 percent of cases), and direct fluorescent-antibody staining of sputum often considered unreliable for species other than *L. pneumophila* [14]. The frequency of infection with *Mycop. pneumoniae* among hospitalized adults with community-acquired pneumonia ranges from 1 percent to 8 percent, and it is much higher for young adults who are treated as outpatients. Diagnostic procedures include serologic tests, culture, and the polymerase chain reaction (PCR) [15]. *Chl. pneumoniae* reportedly accounts for 5 to 10 percent of cases of community-acquired pneumonia. Diagnosis of this agent can be done by serologic testing, culture and by PCR [16].

Viral agents account for 2 to 15 percent of cases, most commonly

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influenza virus and, less commonly, parainfluenza virus and adenovirus. *P. carinii* is not included in most reviews of community-acquired pneumonia, *Mycob. tuberculosis* usually accounts for 1 to 2 percent of cases; its detection is obviously important because of the need both to provide effective therapy and to protect the public health [15].

Symptoms

Several symptoms of acute lower respiratory tract infection may be present, including fever or hyperthermia, rigors, sweats, new cough with or without sputum production or change in the color of respiratory secretions in a patient with chronic cough, chest discomfort or the onset of dyspnoea [4]. Most patients also have nonspecific symptoms such as fatigue, myalgias, abdominal pain, anorexia, and headache. Hospital acquired pneumonia refers to a new episode of pneumonia occurring at least two days after admission to hospital. It is the second most common hospital acquired infection and the leading cause of hospital acquired infection associated death [1].

Many patients who satisfy these criteria do not have pneumonia and failure to distinguish pneumonia from acute bronchitis is an important reason for overuse of antibiotics. Furthermore, CAP can present with fever without localizing features, and some patients may have no fever (elderly patients may present only with a sudden change in functional status) [17].

Thus, if pneumonia is being considered, a chest x-ray is needed. No set of decision rules is as yet superior to clinical judgement when deciding whom to x-ray. Physical signs of consolidation are suggestive but are often not found at presentation. Nevertheless, some clinical signs, such as confusion, should be specifically noted because of their prognostic value [15].

Risk Group

Factors that increase risk of community acquired pneumonia are chronic obstructive pulmonary disease, dementia, heart failure, immunosuppression, age over 50, asthma, alcoholism, indigenous background institutionalisation, seizure disorders, smoking, stroke [17].

Factors that predict increased risk of death from community acquired pneumonia are hypothermia (temperature 37°C), hypotension (systolic blood pressure <100 mmHg), existing neurological disease, more than one lobe involved on chest x-ray, tachypnoea (respiratory rate 20 per min), existing neoplastic disease, leukopenia, confusion, diabetes mellitus, male sex, other factors such as bacteraemia, specific causative organisms such as *Pseudomonas aeruginosa,* Other gram-negative rods (*Escherichia coli*, *Klebsiella* spp.), *Staphylococcus aureus* and *Legionella pneumophila* [15,17].

Pathophysiology of Community Acquired Pneumonia

CAP is a common illness and can affect people of all ages. CAP is usually spread by droplet infection and most cases occurs previously healthy individual. Several factors can impair the effectiveness of local defenses and predispose to CAP. Once the organism settles in the alveoli, an inflammatory response ensues. The classical pathological response evolves through the phases of congestion, red and grey hepatisation and finally resolution with little or no scarring [1].

In pneumonia, the lungs become filled with pus, and this makes them stiff. So the patient breathes fast with stiff lungs. As pneumonia become worse, the lungs become even stiffer and they do not expand properly. Severe pneumonia has a lot of pus in their lungs, so their lungs are very stiff. The sign on which estimation of severity of ALRI is also depend on mediator of inflammation known as acute phase response [1,18].

Laboratory Diagnosis

Chest x-ray

This is the cardinal investigation. In the appropriate setting, a new area of consolidation on chest x-ray makes the diagnosis, but x-ray is a poor guide to the likely pathogen. Other causes of a new lung infiltrate on chest x-ray include atelectasis, non-infective pneumonitis, haemorrhage and cardiac failure. Occasionally, the chest x-ray initially appears normal (eg, in the first few hours of *S. pneumoniae* pneumonia and early in HIV related *P. jiroveci* pneumonia).

Sputum microscopy and culture

There is debate about the value of sputum samples in diagnosis of CAP. Oral flora rather than the offending pathogen may dominate a sputum Gram stain and culture. Nevertheless, we believe that an attempt should be made to obtain a sputum sample before beginning antibiotic therapy, as this is sometimes the best opportunity to identify pathogens that need special treatment.

Blood chemistry and haematology

All patients with CAP being assessed in emergency departments or admitted to hospital should have oximetry, measurement of serum electrolytes and urea levels, and a full blood count to assist in assessing severity. Blood gas measurement is also recommended, as it provides prognostic information (pH and PaO_2) and may identify patients with ventilatory failure or chronic hypercapnia ($PaCO_2$). If the patient has known or suspected diabetes mellitus, measurement of blood glucose also assists in assessing severity.

Blood culture

Blood cultures are the most specific diagnostic test for the causative organism, but are positive in only around 10% of patients admitted to hospital with CAP. The more severe the pneumonia, the more likely blood cultures are to be positive. We recommend that blood be cultured from all patients, except those well enough to be managed at home with oral antibiotics [17].

Other investigations

Serological diagnosis requires acute and convalescent serum samples and is therefore not useful in acute management of CAP. Some laboratories offer acute serodiagnosis for *M. pneumoniae*, but these tests may lack specificity. Even after extensive investigations, the microbial cause of CAP is revealed in only about half of all patients. The most promising are rapid screens that can be performed on throat swabs, using polymerase chain reaction [4,19].

Polymerase Chain Reaction (PCR)

Use of PCR in the field of molecular diagnostics has increased to the point where it is now accepted as the standard method for detecting nucleic acid from a number of sample and microbial types [20].

Treatment

Therapeutic decisions are greatly simplified if the infecting pathogen is known. In general, tests that provide immediate information are desirable such as Gram's staining with or without the quellung test, staining for acid-fast bacilli, direct fluorescent-antibody tests for legionella, or PCR for *Mycop. pneumoniae, Chl. pneumoniae,* and *Mycob. Tuberculosis* [21]. In the absence of guidance from the results of rapid diagnostic tests, recent guidelines for empirical decision making are available from the British Thoracic Society and the American Thoracic Society. These two groups reviewed similar data and recommended quite different regimens. The conclusion of the British Thoracic Society was that empirical therapy should always cover *Strep. pneumoniae*. The preferred regimen is penicillin or amoxicillin; erythromycin should be given if legionella or *Mycop. pneumonia* is specifically suspected and antibiotics directed against *Staph. aureus* should be considered during epidemics of influenza. The American Thoracic Society recommended the use of macrolides, second- and third-generation cephalosporins, trimethoprim–sulfamethoxazole, and beta-lactam–beta-lactamase inhibitors. Agents active against legionella, *Mycop. pneumoniae,* and *Chl. pneumoniae* include new macrolides (clarithromycin and azithromycin), which

are more expensive than erythromycin but better tolerated and more active against *Haem. Influenzae* [22]. About 30 percent of the strains of *Haem. influenzae* produce beta-lactamase and are resistant to ampicillin; most are susceptible to cephalosporins, doxycycline, and trimethoprim–sulfamethoxazole. Fluoroquinolones are effective against atypical agents and *Haem. Influenzae.*

The prevalence of penicillin-resistant *Strep. pneumoniae,* which accounts for over 25 percent of pneumococcal isolates in some areas of the United States and for higher rates in other areas of the world [23-25]. Alternative drugs are limited because of resistance to trimethoprim–sulfamethoxazole, macrolides, and cephalosporins. Most strains have intermediate resistance to penicillin, and uncomplicated pneumonia caused by these strains may be treated with high doses of penicillin or selected cephalosporins, such as cefaclor or cefotaxime [24]. Mortality due to pneumococcal pneumonia involving resistant strains is similar to that for pneumonia involving sensitive strains, even when the treatment includes penicillins or cephalosporins [25].

Most patients with no bacteriologic diagnosis have infections involving atypical agents such as legionella species, *Mycop. pneumoniae,* or *Chl. pneumoniae.* This assumption accounts for the frequent use of macrolides for pneumonia, although studies in outpatients show that macrolides and beta-lactam agents are equally effective in adult outpatients with pneumonia [26]. Legionella is an important pulmonary pathogen that requires treatment with a macrolide or fluoroquinolone, and applies only to hospitalized patients [27].

Adults with community-acquired pneumonia should receive treatment with antibiotic agents selected according to the results of microbiologic studies of sputum and blood cultures. For young adults treated as outpatients, the oral administration of a macrolide (erythromycin, clarithromycin, or azithromycin) or doxycycline; for patients older than 25, oral amoxicillin or an oral cephalosporin is also acceptable. For adults over 60 and those with coexisting illnesses who are treated as outpatients: oral cephalosporin or amoxicillin; for patients with penicillin allergy, oral macrolide or doxycycline. For hospitalized patients: Second- or third-generation cephalosporin (cefuroxime, cefotaxime, or ceftriaxone) with or without erythromycin, given parenterally; parenteral therapy should continue until the patient has been afebrile for more than 24 hours and oxygen saturation exceeds 95 percent [28].

Several medical-specialty professional societies have suggested that combination therapy with a β-lactam plus a macrolide or doxycycline or monotherapy with a "respiratory quinolone" (i.e., levofloxacin, gatifloxacin, moxifloxacin, or gemifloxacin) are optimal first-line therapy for patients hospitalized with community-acquired pneumonia [29]. Combination antibiotic therapy achieves a better outcome compared with monotherapy, and it should be given in the following subset of patients with CAP: outpatients with comorbidities and previous antibiotic therapy, nursing home patients with CAP, hospitalized patients with severe CAP, bacteremic pneumococcal CAP, presence of shock, and necessity of mechanical ventilation [30].

Empiric therapeutic regimens for CAP are outlined below, including those for outpatients with or without comorbidities, intensive care unit (ICU) and non-ICU patients, and penicillin-allergic patients [31].

Outpatient:

- No comorbidities/previously healthy; no risk factors for drug-resistant *S pneumoniae*:

- Azithromycin 500mg PO one dose, then 250mg PO daily for 4 d or extended-release 2g PO as a single dose

or

- Clarithromycin 500mg PO bid or extended-release 1000mg PO q24h or

- Doxycycline 100mg PO bid

- If received prior antibiotic within 3 months:

- Azithromycin or clarithromycin plus amoxicillin 1g PO q8h or amoxicillin-clavulanate 2g PO q12h or

- Respiratory fluoroquinolone (eg, levofloxacin 750mg PO daily or moxifloxacin 400mg PO daily)

- Comorbidities present (eg, alcoholism, bronchiectasis/ cystic fibrosis, COPD, IV drug user, post influenza, asplenia, diabetes mellitus, lung/liver/renal diseases):

- Levofloxacin 750mg PO q24h or

- Moxifloxacin 400mg PO q24h or

Combination of a beta-lactam (amoxicillin 1g PO q8h or amoxicillin-clavulanate 2g PO q12h or ceftriaxone 1g IV/IM q24h or cefuroxime 500mg PO BID) plus a macrolide (azithromycin or clarithromycin)

Duration of therapy: minimum of 5 days, should be afebrile for 48-72 hours, or until afebrile for 3 days; longer duration of therapy may be needed if initial therapy was not active against the identified pathogen or if it was complicated by extrapulmonary infections.

Inpatient, non-ICU:

- Levofloxacin 750mg IV or PO q24h or

- Moxifloxacin 400mg IV or PO q24h or

- Combination of a beta-lactam (ceftriaxone 1g IV q24h or cefotaxime 1g IV q8h or ertapenem 1g IV daily or ceftaroline 600mg IV q12h) plus azithromycin 500mg IV q24h

- Duration of therapy: minimum of 5 days, should be afebrile for 48-72 hours, stable blood pressure, adequate oral intake, and room air oxygen saturation of greater than 90%; longer duration may be needed in some cases.

Inpatient, ICU:

Severe COPD:

- Levofloxacin 750mg IV or PO q24h or

- Moxifloxacin 400mg IV or PO q24h or

- Ceftriaxone 1g IV q24h or ertapenem 1g IV q24h plus azithromycin 500mg IV q24h

If gram-negative rod pneumonia (Pseudomonas) suspected, due to alcoholism with necrotizing pneumoniae, chronic bronchiectasis/ tracheobronchitis due to cystic fibrosis, mechanical ventilation, febrile neutropenia with pulmonary infiltrate, septic shock with organ failure:

- Piperacillin-tazobactam 4.5g IV q6h or 3.375g IV q4h or 4-h infusion of 3.375g q8h or

- Cefepime 2g IV q12h or

- Imipenem/cilastatin 500mg IV q6h or meropenem 1 g IV q8h or

- If penicillin allergic, substitute aztreonam 2g IV q6h plus

- Levofloxacin 750mg IV q24h or

- Moxifloxacin 400mg IV or PO q24h or

- Aminoglycoside (gentamicin 7mg/kg/day IV or tobramycin 7mg/ kg/day IV)

- Add azithromycin 500mg IV q24h if respiratory fluoroquinolone not used

Duration of therapy: 10-14 days

If concomitant with or post influenza:

- Vancomycin 15mg/kg IV q12h or linezolid 600 mg IV bid plus

- Levofloxacin 750mg IV q24h or

- Moxifloxacin 400mg IV or PO q24h

- If received prior antibiotic within 3 months:

- High-dose ampicillin 2g IV q6h (or penicillin G, if not resistant); if penicillin allergic, substitute with vancomycin 1g IV q12h plus

- Azithromycin 500mg IV q24h plus

- Levofloxacin 750mg IV q24h or moxifloxacin 400mg IV/PO q24h

- Risk of aspiration pneumonia/anaerobic lung infection/lung abscess:

- Clindamycin 300-450mg PO q8h or

- Ampicillin-sulbactam 3g IV q6h or

- Ertapenem 1g IV q24h or

- Ceftriaxone 1g IV q24h plus metronidazole 500mg IV q6h or

- Moxifloxacin 400mg IV or PO q24h or

- Piperacillin-tazobactam 3.375g IV q6h or

- If methicillin-resistant *S aureus* (MRSA) is suspected, add vancomycin 15mg/kg IV q12h or linezolid 600mg IV/PO q12h

- If influenza is suspected, add oseltamivir 75mg IV or PO q12h for 5d

Oral fluoroquinolones (ciprofloxacin and ofloxacin) are acceptable alternatives to macrolides for legionnaires' disease, and for *Mycop. pneumoniae* and *Chl. pneumoniae* as well. In areas with high rates of resistance strains of *Strep. pneumoniae,* local sensitivity patterns should be taken into account. The duration of therapy is 5 to 10 days is usually advocated for common bacterial pneumonias, 10 to 14 days for those caused by *Mycop. pneumoniae* or *Chl. pneumoniae,* and 14 to 21 days for legionnaires' disease [22]. Criteria for defining failure to respond are not readily available, although previously healthy adults with pneumococcal pneumonia are usually afebrile within three days [32]. Older patients with pneumococcal pneumonia or bacteremic pneumococcal pneumonia and pneumonia due to gram-negative bacilli, *Staph. aureus,* or legionella usually respond more slowly. Radiographic changes are slow in comparison with the clinical response. Microbiologic tests for common bacterial pathogens in patients with poor responses are generally considered unreliable after antibiotics have been given. Fiberoptic bronchoscopy is often useful for the detection of underlying lesions such as neoplasms, for the detection of selected pathogens such as *Mycob. tuberculosis, P. carinii,* or pathogenic fungi, and occasionally for the detection of *Staph. aureus* or gram-negative bacilli, if quantitative cultures are performed [33]. A computed tomographic scan may identify undetected anatomical changes. Follow-up chest films are most justified for patients with a delayed response, an uncertain cause of pneumonia, or infection with penicillin-resistant *Strep. pneumoniae.* Long-term follow-up radiography is indicated for patients who have delayed responses, for those who may have bronchogenic neoplasms or other underlying disease, and for those with recurrent pneumonia [34].

Prevention

In addition to treating any underlying illness which can increase a person's risk for CAP, there are several ways to prevent CAP. Smoking cessation is important not only for treatment of any underlying lung disease, but also because cigarette smoke interferes with many of the body's natural defenses against CAP.

Vaccination is important in both children and adults. Vaccinations against *Haemophilus influenzae* and *Streptococcus pneumoniae* in the first year of life have greatly reduced their role in CAP in children. A vaccine against *Streptococcus pneumoniae* is also available for adults and is currently recommended for all healthy individuals older than 65 and any adults with emphysema, congestive heart failure, diabetes mellitus, cirrhosis of the liver, alcoholism, cerebrospinal fluid leaks, or

who do not have a spleen. A repeat vaccination may also be required after five or ten years [35].

Influenza vaccines should be given yearly to the same individuals as receive vaccination against *Streptococcus pneumoniae*. In addition, health care workers, nursing home residents, and pregnant women should receive the vaccine. When an influenza outbreak is occurring, medications such as amantadine, remantadine, zanamivir and oseltamivir have been shown to prevent causes of influenza [36].

Conclusion

Prevention of pneumonia is obviously an important goal. Infection with influenza is a critical factor, especially in elderly patients who constitute the adult population group with the highest attack rate for community-acquired pneumonia and the group with the highest mortality due to the disease. *Strep. pneumoniae* continues to be the most common bacterial pathogen in most of the studies of pneumonia and has aroused concern because of the dramatic increase in the rates of resistance to antibacterial agents among isolates. So, we should concern about the current guidelines for the judicious use of antimicrobial agents.

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Akter et al. Int J Respir Pulm Med 2015, 2:1

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