INVITED ARTICLE

COMMUNITY-ACQUIRED PNEUMONIA

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ABSTRACT

Major changes have occurred in the epidemiology of community-acquired pneumonia recently. The emergence of new pathogens emphasises the need for continued vigilance in the diagnosis of pneumonia while changes in the microorganism or in the host have resulted in exciting new aspects of several old pathogens.

Clinical and radiologic signs are unreliable in predicting the infecting organisms. Thus initial therapy is nearly always empiric. This approach often requires good clinical judgement and a knowledge of local epidemiological patterns in choosing an appropriate regimen. State-of-the-art invasive diagnostic procedures are usually reserved for pneumoniae that fail to resolve with initial treatment.

Non-specific measures like stabilisation of underlying medical conditions, adequate nutrition and cessation of smoking or alcohol may help prevent the development of community-acquired pneumonia. On a larger scale, influenza and pneumococcal vaccinations are cost-effective preventive measures.

Keywords: *aetiology, differential diagnoses, empiric therapy, non-resolving, prevention*

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INTRODUCTION

Community-acquired pneumonia (CAP) in the 1990's remains a significant health problem. In the US, pneumonia is the sixth leading cause of death and the number one cause of death due to infections. Despite the introduction of newer antimicrobial agents, vaccines and more sophisticated intensive care facilities, mortality rate associated with pneumonia appears to be increasing for the most recently reported 8-year period (1982-90) after remaining steady during the 1950-60's[1-5].

DEFINITIONS

Infection of the lower respiratory tract are subclassified as pneumonia and bronchitis. Pneumonia is defined as inflammation and consolidation of lung parenchyma due to an infectious agent. In contrast, bronchitis is confined to the bronchial mucosa. CAP refers to pneumonia caused by a pathogen acquired in the community, in contrast to nosocomial pneumonia which is defined as an onset of pneumonia greater than 72 hours following hospitalisation[6].

This review will focus on CAP in immunocompetent individuals only. The increase in the number of organ transplantations and patients infected with the human immunodeficiency virus (HIV) has created a distinct group of patients with CAP of differing aetiologies which require a separate discussion.

MICROBIOLOGICAL AETIOLOGY

Studies on the causative microorganisms in CAP show differing relative frequencies of pathogens as they were carried out in different populations and geographical locations. Results of 2 large studies are shown in Table I[7]. More recent observations include:

1) The relative importance of pneumococcus seems to be decreasing (from > 90% of bacterial pneumoniae in 1960's) while the spectrum of agents causing CAP seems to be expanding.
2) Agents previously considered as non-pathogenic for the respiratory tract (eg *H. influenzae* other than type b, parainfluenza and *Moraxella catarrhalis*) are now identified as pathogens.
3) *Mycoplasma pneumonia* has been increasingly found in age groups other than the young.
4) *Chlamydia pneumoniae* (strain TWAR) is a newly recognised pathogen responsible for lower respiratory tract infections. Chronic Chlamydia pneumonia may also be an independent risk factor for coronary artery disease[8].
5) The emergence of viruses as respiratory pathogens causing serious illnesses, most notably the hanta viruses [(previously known to cause haemorrhagic fever with renal syndrome (HFRS)].

Table I - Causes of Community-Acquired Pneumonia

	Inpatients %*	Outpatients%**
Streptococcus pneumoniae	15.3	9
Haemophilus influenza	10.9	12
Legionella species	6.7	0
Chlamydia species	6.1	4
Mycoplasma pneumoniae	2.0	37
Virus	0.3	14
Unknown	32.9	41

* Percentages add up to less than 100 as some causes are omitted.
** Percentages add up to more than 100 as some patients had two causes.

Locally, a prospective study of the aetiology of adult CAP showed that *Mycobacterium Tuberculosis* (MTB) was the most common pathogen[9]. A similar study conducted in Hong Kong[10] also detected a high percentage of MTB (12%)

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presenting with acute pneumonia. In the US, there is a recent resurgence of tuberculosis with the number of annually reported cases increasing since 1985. More ominously, the rising incidence of multi-drug resistant (MDR) strain has defied control measures by public health authorities.

DIAGNOSIS

Criteria most often used to diagnose pneumonia include a new pulmonary infiltrate on chest X-ray (CXR) plus at least 2 of the following:

1) fever (> 37.8°C oral)
2) leucocytosis (> 10,000/mm^3)
3) production of purulent sputum.

In addition to respiratory symptoms, 10% - 30% of patients with pneumonia complain of headache, nausea, vomiting, abdominal pain, diarrhoea, myalgia and arthralgia[11]. In older patients, signs and symptoms of pneumonia are often incompletely expressed[12]. Fever and leucocytosis occur less often in the elderly. Cerebral symptoms eg confusion, are commonly present.

Differential diagnoses of pneumonia[13,14] include:

1) Bronchiolitis obliterans and organizing pneumonia (BOOP)
2) Eosinophilic pulmonary syndrome - acute eosinophilic pneumonia, chronic eosinophilic pneumonia - allergic bronchopulmonary aspergillosis
3) Hypersensitivity pneumonitis
4) Drug induced pneumonitis eg methotrexate, nitrofurantoin, gold, amiodarone
5) Sarcoidosis
6) Systemic necrotising vasculitis - Churg-Strauss and Wegener's granulomatosis
7) Neoplastic diseases especially pulmonary lymphoma and bronchioloalveolar cell carcinoma
8) Pulmonary embolism.

Radiological diagnosis

Routine CXR on all patients with acute cough cannot be recommended because of its low sensitivity. Rather, CXR should be reserved for patients with abnormal physical signs on chest examination. In most instances, it is impossible to make an aetiologic diagnosis based on CXR appearance alone. However, pattern recognition may occasionally be helpful in suggesting the aetiologic agent (Table II)[1].

Microbiological diagnosis

The history and physical examination can provide important clues to the aetiology of pneumonia (Table III)[1]. The term atypical pneumonia, first introduced in 1938, refers to pneumonia in which none of the usual bacterial causes are evident. Instead, the following organisms are possible causes: *Mycoplasma pneumoniae, Chlamydia psittaci, Chlamydia pneumoniae* (strain TWAR), *Coxiella burnetii, Francisella tularensis, Histoplasma capsulatum, Coccidioides immitis* and certain viruses[15]. It was previously thought that atypical pneumoniae differed from "typical bacterial" pneumoniae in the following ways:

1) systemic symptoms are more pronounced than respiratory complaints,
2) patient does not appear acutely ill or toxic,
3) onset is insidious rather than abrupt,
4) cough is unproductive,
5) leucocytosis is usually absent,
6) hilar/segmental lower lobe infiltrates are seen on CXR.

Recent studies, however, have shown that distinction between typical bacterial and atypical pneumonia based on clinical features alone is difficult[3,16].

Table II - Possible microbial causes associated with various radiographic patterns

Focal Opacity *S. pneumoniae* *M. pneumoniae* *L. pneumophila* *S. aureus* *C. pneumoniae* *M. tuberculosis*	**Multi-focal opacities** *S. Aureus* *C. burnetii* *L. pneumophila* *S. pneumoniae*
Interstitial Viruses *M. pneumoniae* *P. carinii* *C. psittaci*	**Miliary** *M. tuberculosis* *H. capsulatum* *C. immitis* Varicella zoster
Interstitial, with lymphadenopathy Epstein-Barr virus *M. pneumoniae* *C. psittaci*	**Segmental or lobar, with lymphadenopathy** *M. tuberculosis* (primary infection) Fungi
Cavitation Mixed aerobic/anaerobic organisms (lung abscess) Aerobic gram-negative bacilli *M. tuberculosis* *L. pneumophila* Fungi	**Pneumatocoeles** *S. aureus* *S. pyogenes* *P. carinii*
Bulging fissure *K. pneumoniae* *L. Pneumophila*	**Round lesions** *C. burnetii* *S. pneumoniae* *L. pneumophila* *S. aureus*

TESTS TO DETERMINE AETIOLOGY

Sputum gram stain and cultures

The value of sputum gram stain examination is debatable. Specimens containing > 10 epithelial cells per low power field are likely to represent oropharyngeal contamination and should be discarded. Elastin fibres visualised in a potassium hydroxide (KOH) preparation of expectorated sputum were found to be a sensitive indicator of lung necrosis in patients with pneumonia[17]. The limitations of sputum gram stain examination are:

1) a good quality sputum is often unattainable,
2) gram stain is unable to detect many common respiratory pathogens eg *M. pneumoniae, C, pneumoniae,* respiratory viruses,
3) expertise in interpretation is required (normal flora eg viridans streptococcus may be mistaken for pneumococcus).

Conversely, sputum examination is useful in the following ways:

1) the finding of a preponderance of gram positive lancet-shaped diplococcus associated with polymorphonuclear leucocytes is approximately 60% sensitive and 90% specific for the diagnosis of pneumococcal pneumonia,
2) more sophisticated tests eg direct fluorescent antibody testing are available for some respiratory pathogens eg *Legionella pneumophila* and results are specific and rapidly available.
3) assays to detect pneumococcal capsular antigens in sputum are also available.

Overall, positive sputum cultures may represent upper airway colonisation. Therefore, they should be interpreted together with gram stain results.

Table III - Clues to the aetiology of pneumonia from the medical history and physical examination findings.

Features	Possible aetiologic organism(s)
Environmental factor	
Exposure to contaminated air-conditioning cooling towers, recent travel and stay in a hotel, exposure to grocery store mist machine, or visit to or recent stay in a hospital with contaminated (by *L. pneumophila)* drinking water	*Legionella pneumophila*
Exposure to infected parturient cats, cattle, sheep or goats	*Coxiella burnetii*
Pneumonia develops after windstorm in an area of endemicity	*Coccidioides immitis*
Outbreak of pneumonia occurs in shelter for homeless men or jail	*Streptococcus pneumoniae, Mycobacterium tuberculosis*
Outbreak of pneumonia occurs in military training camp	*S. pneumoniae, Chlamydia pneumoniae*
Animal contact	
Exposure to contaminated bat caves, excavation in areas of endemicity	*Histoplasma capsulatum*
Exposure to turkeys, chickens, ducks, or psittacine birds	*Chlamydia psittaci*
Travel history	
Travel to Thailand or other countries in Southeast Asia	*Pseudomonas Pseudomallei (melioidosis)*
Immigration from Asia or India	*M. tuberculosis*
Occupational history	
Health care worker who works with patients infected with human immunodeficiency virus (HIV) in a large city	*M. tuberculosis*
Host factor	
Diabetic ketoacidosis	*S. pneumoniae, Staphylococcus aureus*
Alcoholism	*S. pneumoniae, Klebsiella pneumoniae, S. aureus*
Chronic obstructive lung disease	*S. pneumoniae, Haemophilus influenzae, Moraxella catarrhalis*
Solid organ transplant recipient (pneumonia occurs > 3 months after transplant)	*S. pneumoniae, H. influenzae, Legionella* species, *Pneumocystis carinii*, cytomegalovirus, *Strongyloides stercoralis*
Sickle cell disease	*S. pneumoniae*
HIV infection and CD4 cell count of <200/uL	*P. carinii, S. pneumoniae, H.influenzae, Cryptococcus neoformans, M. tuberculosis, Rhodococcus equi*
Physical findings	
Periodontal disease with foul-smelling sputum	Anaerobes and aerobes
Bullous myringitis	*Mycoplasma pneumoniae*
Absent gag reflex, altered level of consciousness, or recent seizure	Polymicrobial (oral aerobic and anaerobic bacteria, macroaspirated or microaspirated)
Encephalitis	*M. pneumoniae, C. burnetii, L. pneumophila*
Cerebellar ataxia	*M. pneumoniae, L. pneumophila*
Erythema multiforme	*M. pneumoniae*
Erythema nodosum	*C. pneumoniae, M. tuberculosis*
Ecthyma gangrenosum	*Pseudomonas aeruginosa, Serratia marcescens*
Cutaneous nodules (abscesses) and CNS abnormalities	*Nocardia species*

Blood cultures and cultures from infected fluid
All hospitalised patients with CAP should have 2 sets of blood cultures performed (aerobic and anaerobic). Eight to ten percent of such blood cultures yield positive results. Pneumococci account for 60% of cases of bacteraemic CAP. Aspiration of infected pleural fluid may also yield the aetiologic agent.

Serology for specific pathogens (eg *Mycoplasma pneumoniae, Chlamydia pneumoniae, Coxiella burnetii, Legionella pneumophila)*
This is helpful in epidemiologic studies but diagnosis is based on the detection of a 4-fold rise in serum antibody titres between acute and convalescent sera, thus limiting its usefulness in directing initial therapy. Serology also lacks sensitivity and specificity. Therefore serological testing should not be done routinely on all patients with CAP.

Invasive techniques
These techniques are designed to enable sampling of respiratory secretions in patients who cannot produce sputum and to obtain specimens not contaminated by oropharyngeal flora.

a) ***Transtracheal aspiration***
Its overall sensitivity is high (80% in some series) but specificity is low[18,19]. Although complications are rare, its use has decreased mainly because it is often not very acceptable to patients.

b) ***Transthoracic needle aspiration***
Sensitivity varies from 60% - 90% and specificity is almost 100%[20]. With the use of ultrathin needles, complication rate of the technique is extremely low.

c) ***Protected specimen brushing (PSB) and bronchoalveolar lavage (BAL)***

These procedures require bronchoscopy. The diagnostic yield is high (up to 70%) if carried out prior to the initiation of antibiotics. If performed because the patient's condition has not improved following > 72 hours of antibiotic therapy, the microbiological yield is much lower[21].

d) ***Open lung biopsy***

This is only rarely necessary. In general, invasive techniques are only required when patients are not responding to empiric therapy. Despite extensive testing, the responsible pathogen is not defined in as many as 50% of patients with CAP[1,3].

ANTIMICROBIAL THERAPY

By necessity, most patients are initially treated with an empiric antimicrobial regime pending results from diagnostic studies. Factors to consider in choosing an antibiotic are[22]:

1) organism - likely causative pathogen, antibiotic resistance pattern,
2) patient - severity of illness, antibiotic hypersensitivity,
3) antibiotic - penetration into respiratory tract, effectiveness in clinical studies, interactions with other drugs, cost.

Current guidelines for antibiotic choice in the initial management of adults with CAP are provided by the American Thoracic Society (Table IV - VII[23]).

Table IV - Management of outpatient pneumonia without comorbidity and 60 years of age or younger

Organisms
S.pneumoniae
M. pneumoniae
Respiratory viruses
C. pneumoniae
H. influenzae
Miscellaneous
Legionella sp., *S. aureus, M tuberculosis*, endemic fungi, aerobic gram-negative bacilli
Therapy
Macrolide
OR
Tetracycline

Table V - Management of outpatient pneumonia with comorbidity and/or 60 years of age or older

Organisms
S. pneumoniae
Respiratory viruses
H. influenzae
Aerobic gram-negative bacilli
S. aureus
Miscellaneous
Moraxella catarrhalis, Legionella sp., *M. tuberculosis*, endemic fungi
Therapy
Second generation cephalosporin
OR
TMP/SMX
OR
Beta-lactam/beta-lactamase inhibitor
±
Erythromycin or other macrolide

Table VI - Management of hospitalised patients with community-acquired pneumonia

Organisms
S. pneumoniae
H. influenzae
Polymicrobial (including anaerobic bacteria)
Aerobic gram-negative bacilli
Legionella sp.
S. aureus
C. pneumoniae
Respiratory viruses
Miscellaneous
M. pneumoniae, Moraxella catarrhalis, M. tuberculosis, endemic fungi
Therapy
Second or third generation cephalosporin
OR
Beta-lactam/beta-lactamase inhibitor
±
Macrolide

Table VII - Management of severe hospitalised community-acquired pneumonia

Organisms
S pneumoniae
Legionella sp.
Aerobic gram-negative bacilli
M. pneumoniae
Respiratory viruses
Miscellaneous
H. influenzae, M tuberculosis
Endemic fungi
Therapy
Macrolide
PLUS
Third generation cephalosporin with anti-Pseudomonas activity
OR
Other antipseudomonal agents such as imipenam/ cilastatin, ciprofloxacin

Inpatient versus outpatient treatment

Risk factors that increase either the risk of death or a complicated course of CAP are depicted in Table VIII[23,24]. These criteria should complement rather than supplant clinical judgement regarding hospitalisation needs of patients with CAP. At least as important as the above risk factors is the need for the physician to assess whether the patient has functional skills and social support to care for himself outside the hospital and the ability to comply with treatment[7]. Other aspects of treatment which need to be attended to include adequate oxygenation and hydration, management of a parapneumonic pleural effusion or empyema[25], control of atrial arrhythmias and treatment of hyponatremia (secondary to SIADH).

Slowly/Non resolving pneumonia

Abnormal physical signs can persist beyond 7 days in 20% - 40% of patients. CXR abnormalities clear much more slowly and the rate of resolution is dependent on the age of the patient, number of lobes involved[26], presence of bacteraemia, underlying comorbid illness and the inciting agent. Elderly patients with CAP may take up to 6 months for complete radiological resolution. If response is slow, there is clinical deterioration or worsening of chest radiograph (as defined by a 50% or greater increase in size of infiltrates, progression to involvement of

multiple lobes or development of a large pleural effusion)[27], the patient should be reevaluated and the possible cause(s) elucidated (Table IX)[28]. Microbiologic studies should be repeated - blood cultures, urine cultures, sputum specimens. CT thorax is useful in identifying an unsuspected pleural effusion, obstructing mass, lymphadenopathy, bronchiectasis, congenital abnormalities eg sequestration, and in guiding percutaneous needle biopsy. Invasive investigations may be considered at this stage. Finally, if CAP caused by the identified pathogen is not responding to treatment, resistance must be considered. Many bacterial resistance patterns are stable but wide geographical variations occur, including penicillin-resistant pneumococcus (S Africa, Spain, Hungary) and ampicillin-resistant *Haemophilus influenzae* (Spain, France, Belgium)[14].

RECURRENT PNEUMONIA

This term refers to the occurrence of two or more episodes of pneumonia that are separated by an interval during which the radiograph opacity completely clears or symptoms disappear totally for at least one month[2]. Differential diagnoses include bronchiectasis, chronic obstructive pulmonary disease and congestive heart failure.

Table VIII - Risk factors associated with a complicated course of CAP

Coexisting illness/conditions
Age > 60
COPD
Diabetes mellitus
Chronic renal failure
Chronic liver disease
Hospitalisation within past year for CAP
Ethanol abuse
Suspicion of aspiration
Altered mental status
Postsplenectomy state
Malnutrition
Severity of illness at presentation
Findings on clinical examination
Oral temperature > 100°F
Respiratory rate > 30 bpm
Systolic BP ≤ 90 mmHg
Diastolic BP ≤ 60 mmHg
Metastatic infectious sites
Delirium
Laboratory findings
WBC > 30,000 or < 4,000 cells/mm^3
Hct < 30% or Hb < 9g/dl
Need for mechanical ventilation
ABG on room air: PaO_2 < 60 or $PaCO_2$ > 50 mmHg
Creatinine > 1.2 or BUN > 20 mg/dl
Laboratory evidence of
Sepsis
DIC
Organ dysfunction (ie renal, hepatic)
Chest X-ray findings
Multilobar infiltrates
Cavitation
Pleural effusions
Rapidly spreading infiltrates

PREVENTION

Influenza and pneumococcal vaccinations are cost effective measures against CAP, especially for certain target groups (Tables X & XI)[29]. These vaccinations are, however, currently grossly underutilised.

PROGNOSIS

Specific risk factors for mortality or a complicated course of CAP have been described (Table VIII). In addition, Fine[30] evaluated risk factors prospectively - a numerical value was determined for each of the 6 risk factors based on a mortality risk ratio (Table XII). Why the presence of pleuritic chest pain is associated with low mortality rate is unknown. High risk pathogens are gram negative rods, *S. aureus,* and those complicating aspiration and post obstructive pneumonia. Death is a rare outcome of pneumonia due to *M. pneumoniae* or *C. burnetii.*

Table IX – Causes of treatment failure of CAP

Reason for failure	Examples
Incorrect diagnosis	Pulmonary embolism,pulmonary oedema, pulmonary eosinophilia, Wegener's granulomatosis
Resistant organisms	Ampicillin-resistant *Haemophilus influenzae,* resistance developing during treatment
Resistant infection	*M. pneumoniae, C. psittaci, C. burnetii, S. aureus,* unrecognised pulmonary TB, fungi, viruses
Unrecognised immunodeficiency	HIV infection leading to PCP
Complication	Empyema, abscess, pulmonary embolism fever related to drug therapy, superinfection
Underlying disease	Lung cancer, cardiac failure

Table X - Target groups for influenza vaccination programme

Persons at increased risk for flu-related complications
Persons > 65 years of age
Residents of chronic care facilities housing persons of any age with chronic medical conditions
Persons with chronic cardiopulmonary disease including children with asthma
Persons requiring regular medical care for chronic diseases, including diabetes mellitus, renal dysfunction, hemoglobinopathies or immunosuppression (eg HIV)
Persons who can transmit influenza to high-risk persons
Health care workers (physicians, nurses)
Nursing home and long-term care facility employees in contact with high-risk persons
Household members and home-care providers (eg visiting nurses, volunteers)
Others groups
General population - any person who wishes to lessen their chance of acquiring influenza infection
Essential community services providers; foreign travellers
Pregnant women who have medical conditions that increase their risk of complication from influenza

Table XI - High-risk persons who should receive pneumococcal vaccine

Patients > 65 years of age
Chronic cardiac disease (eg congestive heart failure)
Chronic pulmonary disease (COPD, chronic bronchitis)
Anatomic or functional asplenia
Chronic liver disease
Alcoholism
Diabetes mellitus
Chronic renal failure
Hodgkin's disease
Chronic lymphocytic leukemia
Multiple myeloma
Chronic haemodialysis
HIV infection

Table XII - Risk factors predictive of outcome

Risk factor	Value for risk factor
Pleuritic chest pain	-2
Age > 65	+1
Mental status change	+2
Vital sign abnormality	+2
High risk pathogen	+2
Neoplastic disease	+4

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