Antimicrobial treatment of community acquired pneumonia in adults: A conference report

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COMMUNITY ACQUIRED PNEUMONIA REPRESENTS A MAJOR medical problem. This is despite advances in our understanding of the etiology, epidemiology and pathogenesis of the disease as well as the availability of numerous types of antimicrobials. For those cases requiring admission to hospital, the overall mortality rate can exceed 20% (1).

Since community acquired pneumonia is not a reportable disease, it is difficult to obtain accurate statistics on its true incidence. Figures from the United States suggest that approximately 3.3 million cases occur annually in ambulatory patients. Data from England support an incidence of one to three cases of pneumonia per 1000 adults per year while in Sweden, the incidence is five per 1000. To complicate matters further, it is often difficult to identify the etiological pathogen. Pneumonia and influenza are among the leading causes of death in Americans aged 65 years or older (2).

DEVELOPMENT OF GUIDELINES

In order to develop a standardized approach to the antimicrobial treatment of community acquired pneumonia in Canada, a meeting was held in Halifax, Nova Scotia in November 1991. The participants were

Chairmen of Working Groups: Dr LA Mandell, Dr T Marrie, Dr V Yu

Other participants: Dr M Fleming, Dr K Forward, Dr R Gleckman, Dr R Gold, Dr M Gribble, Dr R Grossman, Dr J MacFarlane, Dr LE Nicolle, Dr M Niederman, Dr A Ortqvist, Dr G Sarosi, Dr W Schlech, Dr P Turgeon, Dr A Verghese, Dr M White

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physicians with a variety of backgrounds including family practice, infectious diseases, microbiology and respirology. Experts from Canada, the United States, England and Sweden attended, all with a particular interest in respiratory tract infections. The guidelines presented in this paper are a representation of the opinions of these experts.

These guidelines were developed solely to help in the **initial antimicrobial management** of patients with community acquired pneumonia. **They are neither definitive nor all encompassing but are meant solely to provide the practising physician with a rational approach to the initial treatment** of community acquired pneumonia and are based upon careful consideration of etiological and epidemiological factors and, above all, the safety and welfare of the patient. Whenever possible, attempts should be made to establish a precise etiological diagnosis. In cases where a specific pathogen is identified, therapy may be specifically targeted using an antimicrobial with a relatively narrow spectrum of activity to which the organism is sensitive. In choosing any antimicrobial, once issues of efficacy and toxicity have been addressed, cost should then be considered.

In developing these guidelines, it was felt that to be workable they must be kept as practical and as simple as possible. Trying to encompass every eventuality would lead to overly complex guidelines that ultimately would be discarded. Accordingly, we have chosen not to deal with the issue of tuberculosis or with high risk patients, such as those with human immunodeficiency virus infection, neoplastic disease or immunosuppressed patients. Such patients generally tend to be managed by physicians with specific expertise in these

TABLE 1
Treatment options for community acquired pneumonia
Clinical presentation – not severe
Treatment – as outpatient oral therapy or inpatient therapy

	Patient previously well and/or <65 years old	Comorbid illness and/or >65 years old
Organisms	<i>Streptococcus pneumoniae</i> <i>Mycoplasma pneumoniae</i> <i>Chlamydia pneumoniae</i> <i>Haemophilus influenzae</i>	<i>Strep pneumoniae</i> <i>H influenzae</i> Oral anaerobes Gram-negative rods <i>Staphylococcus aureus</i> <i>Legionella</i> species
Drugs	1. Macrolide 2. Tetracycline*	1. 2nd generation cephalosporin 2. Trimethoprim/sulphamethoxazole 3. Penicillin plus beta-lactamase inhibitor } ± macrolide [†]

*Some pneumococci are resistant to tetracycline; recommendations will be altered as newer agents become available. [†]If *Legionella* is a concern

TABLE 2
Treatment options for community acquired pneumonia
Clinical presentation – severe
Treatment – in hospital

	Hospital ward		Intensive care unit	
	No comorbidity	Comorbidity	No comorbidity	Comorbidity
Organisms	<i>Streptococcus pneumoniae</i> <i>Legionella</i> species <i>Haemophilus influenzae</i> <i>Mycoplasma pneumoniae</i> <i>Staphylococcus aureus</i> <i>Chlamydia pneumoniae</i>	<i>Strep pneumoniae</i> <i>H influenzae</i> Gram-negative rods Oral anaerobes <i>Legionella</i> species <i>Staph aureus</i>	<i>Strep pneumoniae</i> <i>Legionella</i> species <i>H influenzae</i> Gram-negative rods (including <i>Pseudomonas aeruginosa</i> *) <i>M pneumoniae</i> <i>Staph aureus</i> [†] <i>C pneumoniae</i>	<i>Strep pneumoniae</i> <i>H influenzae</i> Gram-negative rods (including <i>P aeruginosa</i> *) <i>Legionella</i> species <i>Staph aureus</i> [†]
Drugs	2nd or 3rd generation cephalosporin ± macrolide ± rifampin In penicillin-allergic patients – trimethoprim/sulpha- methoxazole plus macrolide		Macrolide ± rifampin plus 3rd generation cephalosporin with antipseudomonas activity or imipenen/cilastatin or ciprofloxacin	

*Due to the high mortality associated with *P aeruginosa*, an aminoglycoside should be added at least for the first few days, whether one uses a third generation cephalosporin, imipenen or ciprofloxacin. [†]First-line cover for *S aureus* (oxacillin-sensitive) is a penicillinase-resistant semisynthetic penicillin; however, the regimens listed above, while not optimal, would provide reasonable cover until identification and sensitivities of the pathogens were determined, at which time therapy may be altered

areas. Since insufficient data exist on the true incidence of viral causes of community acquired pneumonia, we have excluded viruses from these guidelines.

APPROACH TO PNEUMONIA

Although a variety of classifications of pneumonia exist, we have chosen to base our approach to treatment upon the following four variables:

- The severity of illness upon clinical presentation
- Whether the pneumonia was acquired in the community setting itself or in a nursing home
- The presence or absence of comorbid illness (or age older than 65 years)
- Whether treatment is to be given in the community setting, the nursing home or following admission of the patient to a hospital.

While an absolute definition of severity of illness is

not possible, some general guidelines can be provided. Criteria for 'severe pneumonia' include patients presenting with any of the following: respiratory failure ($\text{PaO}_2 < 60$ mmHg [with the exception of patients with chronic obstructive lung disease who may be hypoxemic without pneumonia]); respiratory rate more than 30/min; sepsis with evidence of end organ dysfunction; extrapulmonary septic complications; cavitation or involvement of more than one lobe on chest radiograph (3-5).

Comorbid illness is defined as chronic obstructive lung disease, diabetes mellitus, renal insufficiency, congestive heart failure or recent hospitalization within one year of the presentation with pneumonia (6). Other medical conditions may also exist that might be construed as comorbid conditions. The attending physician's clinical judgement should be used in assessing such cases.

TABLE 3
Treatment options for nursing home acquired pneumonia
Clinical presentation – not severe
Treatment – in nursing home

	Comorbid illness and/or > 65 years
Organisms	<i>Streptococcus pneumoniae</i> <i>Haemophilus influenzae</i> Oral anaerobes Gram-negative rods <i>Staphylococcus aureus</i> <i>Legionella</i> species
Drugs	1. 2nd generation cephalosporin 2. Trimethoprim/sulphamethoxazole 3. Amoxicillin/clavulanate } ± macrolide*

*If *legionella* is a concern

TABLE 4
Treatment options for nursing home acquired pneumonia
Clinical presentation – severe
Treatment – in nursing home*

	Nursing home
Organisms	<i>Streptococcus pneumoniae</i> <i>Haemophilus influenzae</i> Oral anaerobes Gram-negative rods <i>Staphylococcus aureus</i> <i>Legionella</i> species
Drugs	Penicillin plus ciprofloxacin (oral) or 2nd generation cephalosporin ± macrolide (oral) or ceftriaxone (intramuscular) ± macrolide (oral) In penicillin-allergic patients Ciprofloxacin plus clindamycin (intramuscular)

*If patient is to be transferred to hospital for treatment, see Table 2

An approach which incorporates these factors allowed consideration of the greatest number of variables that might impact upon the treatment as well as the prognosis of the individual patient. We specifically avoided the use of a syndrome approach since there can be considerable overlap in clinical symptoms and physical signs, especially in the elderly (7). These guidelines presuppose that in all cases, the individual physician dealing with the patient is the best judge of what to do. In all cases, knowledge of local epidemiology and resistance patterns should be used to modify these guidelines where appropriate.

Based upon the variables mentioned above, the various treatment options are presented in Tables 1, 2, 3 and 4. We have tried to use classes of drugs rather than individual agents whenever possible. However, if only one drug in a given class is available or felt to be suitable, then a specific drug name has been used. Tables 1 and 2 deal with patients who have acquired

APPENDIX

Drug class	Individual agents
I. Beta-lactams	
a) Penicillins	Penicillin G Phenoxymethyl penicillin Amoxicillin/clavulanic acid (oral) Ticarcillin/clavulanic acid (iv)
b) Penicillins plus beta-lactamase inhibitors	
c) Cephalosporins	
2nd generation	Cefuroxime Cefamandol Ceftriaxone Cefotaxime Ceftazidime Cefoperazone*
3rd generation	
3rd generation with anti-pseudomonas activity	
d) Carbapenem	Imipenem/cilastatin
II. Macrolides	Erythromycin Clarithromycin
III. Lincosamides	Clindamycin
IV. Fluoroquinolones	Ciprofloxacin Ofloxacin*
V. Aminoglycosides	Gentamicin Tobramycin
VI. Rifamycins	Rifampin
VII. Tetracyclines	Tetracycline
VIII. Miscellaneous	Trimethoprim/sulphamethoxazole

*Less active against *Pseudomonas aeruginosa* than other drug in its class

pneumonia in the community setting and who present with clinical pictures that are not severe and severe, respectively. Tables 3 and 4 deal with patients with nursing home acquired pneumonia which are not severe and severe, respectively. The practice of transferring patients from a nursing home to a hospital depends upon a variety of social and economic factors and varies from province to province within Canada and from country to country outside Canada.

Most patients with community acquired pneumonia do not need to be admitted to hospital. Of those that do require admission, not all are necessarily severely ill. Of the four tables, Table 1 perhaps applies to the largest percentage of patients.

For patients admitted to hospital, close follow-up is assured but for patients treated at home, follow-up at two to three days is important. In all cases, whenever additional information, such as culture and sensitivity data which may impact treatment comes to light, the responsible physician should make any necessary modifications or adjustments to the initial treatment regimen.

There is no single approach to the diagnosis and treatment of pneumonia that will suffice under all circumstances. What we are using here is an approach that allows for the initial selection of empiric antimicrobial therapy.

While penicillin is the drug of choice for infection caused by sensitive strains of *Streptococcus pneumo-*

niae, it does not provide cover for pathogens such as *Mycoplasma pneumoniae*, *Legionella pneumophila* and *Chlamydia pneumoniae*. Erythromycin, which has excellent activity against the latter three pathogens, is essentially ineffective against *Haemophilus influenzae*. To confound the situation further, beta-lactamase production by *H influenzae* and *Moraxella catarrhalis* makes routine use of ampicillin or amoxicillin unwise (8). Obviously, if a proper sputum sample shows many polymorphonuclear leukocytes and Gram-positive diplococci on Gram stain, penicillin would be the agent of choice. In many situations, however, the decisions are not as clear cut and it is for such situations that these guidelines are intended. As newer antimicrobials become available or as the epidemiology of responsible pathogens changes, these guidelines will be updated.

At present it is recommended that the diagnostic work-up of a patient with known or suspected pneumonia include a careful history, including identification of any comorbid conditions, and a thorough physical examination.

One should also attempt to obtain a proper sputum sample for Gram stain and culture as well as blood samples for a white blood cell count and differential, serology (*Legionella* species, *M pneumoniae*, *C pneumoniae*) and a posterior-anterior and lateral chest radiograph (9). Blood cultures should also be taken routinely from patients who are to be admitted to hospital.

In all cases, consideration must also be given to ancillary modes of treatment where appropriate, including respiratory support, positioning of the patient and management of complications.

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