Summary of Canadian Guidelines for the Initial Management of Community-acquired Pneumonia: An evidence-based update by the Canadian Infectious Disease Society and the Canadian Thoracic Society

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ORIGINAL ARTICLE


Community-acquired pneumonia (CAP) is a serious illness with a significant impact on individual patients and society as a whole. Over the past several years, there have been significant advances in the knowledge and understanding of the etiology of the disease, and an appreciation of problems such as mixed infections and increasing antimicrobial resistance. The development of additional fluoroquinolone agents with enhanced activity against *Streptococcus pneumoniae* has been important as well.

It was decided that the time had come to update and modify the previous CAP guidelines, which were published in 1993. The current guidelines represent a joint effort by the Canadian Infectious Diseases Society and the Canadian Thoracic Society, and they address the etiology, diagnosis and initial management of CAP. The diagnostic section is based on the site of care, and the treatment section is organized according to whether one is dealing with outpatients, inpatients or nursing home patients.

Key Words: Canada; Community-acquired pneumonia; Guidelines
Community-acquired pneumonia (CAP) remains a serious illness with a significant impact not only on individual patients but on society as a whole. Guidelines for the initial antibiotic management of CAP were developed in Canada in 1993 (1), and subsequently by the American Thoracic Society (ATS) that same year (2) and the Infectious Diseases Society of America (IDSA) in 1998 (3). Each set of guidelines has its own strengths and weaknesses, but individually and collectively they have helped to organize and codify our approach to the patient with CAP. Perhaps most importantly, they have highlighted the weaknesses and deficiencies in this area, and have raised important questions for present and future research.

As a result of the developments that have taken place in the past several years, it became clear that the Canadian guidelines needed to be updated and revised. The present document is a joint effort of the Canadian Infectious Diseases Society (CIDS) and the Canadian Thoracic Society (CTS), and is hopefully the first of many such collaborations. This paper is the shortened version of the manuscript, with the key tables and figures included. Readers interested in the more extensive document are referred to the August 2000 issue of Clinical Infectious Diseases (4). These guidelines are evidence based. A hierarchical evaluation of the strength of evidence, modified from the Canadian Task Force on the Periodic Health Examination (5), was used. Well-conducted randomized, controlled trials constitute strong or level I evidence; well-designed, controlled trials without randomization (including cohort and case-control studies) constitute level II or fair evidence; and expert opinion, case studies, and before and after studies are level III (weak) evidence.

CAP, together with influenza, is the sixth leading cause of death in the United States, with an estimated four million cases occurring annually. It accounts for 600,000 hospital admissions and 64 million days of restricted activity/year in the United States (6,7). The risk factors for pneumonia in individuals 60 years of age and older are the following: alcoholism – relative risk (RR) 9.0; asthma – RR 4.2; immunosuppression – RR 1.9; institutionalization – RR 1.8; and 70 years of age and older compared with 60 to 69 years of age – RR 1.5 (8). For pneumococcal infections, the following risk factors have been described: dementia, seizure disorders, congestive heart failure, cerebrovascular disease and chronic obstructive pulmonary disease (COPD) (9).

**TABLE 1**

<table>
<thead>
<tr>
<th>Reference</th>
<th>Location</th>
<th>Date</th>
<th>N</th>
<th>S pneum</th>
<th>H influen</th>
<th>M pneum</th>
<th>C pneum</th>
<th>Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>Goteborg, Sweden</td>
<td>3 years*</td>
<td>54</td>
<td>9 (9)</td>
<td>6 (12)</td>
<td>20 (37)</td>
<td>ND</td>
<td>41%</td>
</tr>
<tr>
<td>13</td>
<td>Halifax, Nova Scotia</td>
<td>November 1991 to March 1994</td>
<td>149</td>
<td>1</td>
<td>1</td>
<td>34 (22.8)</td>
<td>16 (10.7)</td>
<td>48%</td>
</tr>
<tr>
<td>14†</td>
<td>Neuchatel, Switzerland</td>
<td>4 years*</td>
<td>161</td>
<td>17 (11)</td>
<td>3 (2)</td>
<td>28 (17.4)</td>
<td>ND</td>
<td>47%</td>
</tr>
<tr>
<td>15†</td>
<td>Amherst, Nova Scotia</td>
<td>July 1989 to June 1990</td>
<td>75</td>
<td>–</td>
<td>–</td>
<td>22 (29)</td>
<td>1 (5.3)</td>
<td>55%</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td>439</td>
<td>23 (5)</td>
<td>10 (2.3)</td>
<td>104 (24)</td>
<td>211 (48%)</td>
<td></td>
</tr>
</tbody>
</table>

*Start and stop dates not available; †8.7% required hospitalization in Erard et al’s study (14), 35% in Langille et al’s study (15). C pneum Chlamydia pneumoniae; H influen Haemophilus influenzae; M pneum Mycoplasma pneumoniae; ND No data; S pneum Streptococcus pneumoniae.
Pseudomonas aeruginosa, Haemophilus influenzae, Moraxella catarrhalis, Enterobacteriaceae or Staphylococcus aureus infection is defined as the isolation of a pathogen from blood or pleural fluid with a fourfold or greater rise in an antibody titre to Legionella pneumophila, Mycoplasma pneumoniae or Chlamydia pneumoniae from purulent sputum (sputum with moderate or large numbers of neutrophils seen on Gram stain) in which a compatible organism was seen in moderate or large amounts on sputum Gram stain.

Possible infection is defined as the isolation of pneumonia pathogens other than Legionella species from a culture of purulent sputum seen on a Gram stain: predominance of Gram-positive diplococci (possible diagnosis of infection with Staphylococcus pneumoniae assigned) or Gram-positive cocci in clusters (possible diagnosis of infection with Staphylococcus aureus assigned), indicative of possible infection due to either of these agents; an antibody titre of 1:1024 or greater to Legionella species in either the acute or convalescent phase serum; an antibody titre of 1:64 or greater to Mycoplasma pneumoniae; or an immunoglobulin (Ig) G antibody titre of 1:512 or greater, or an IgM antibody titre of 1:16 or greater to Chlamydia pneumoniae. CAP is not a homogeneous entity, and it is useful to consider its etiology according to the following:

- **site of acquisition of pneumonia** – community at large, nursing home;
- **site of care** – outpatients, inpatients, intensive care unit, nursing home;
- **immune status** – exogenous immunosuppression or human immunodeficiency virus (HIV) infection; and
- **specific comorbid illness** such as COPD.

### TABLE 2

<table>
<thead>
<tr>
<th>Reference</th>
<th>Location</th>
<th>Date</th>
<th>N</th>
<th>S pneumonia</th>
<th>H influenza</th>
<th>S aureus</th>
<th>L pneumonia</th>
<th>M pneumonia</th>
<th>C pneumonia</th>
<th>AGNR</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>Halifax, Nova Scotia, Canada</td>
<td>November 1981</td>
<td>278</td>
<td>52 (8.8)</td>
<td>26 (4.4)</td>
<td>22 (3.7)</td>
<td>14 (2.3)</td>
<td>39 (6.6)</td>
<td>–</td>
<td>19 (3.2)</td>
</tr>
<tr>
<td>16</td>
<td>Pittsburgh, USA</td>
<td>July 1986 to March 1987</td>
<td>365</td>
<td>55 (15.3)</td>
<td>39 (10.9)</td>
<td>12 (3.3)</td>
<td>22 (6)</td>
<td>7 (2)</td>
<td>22 (6.1)</td>
<td>21 (5.9)</td>
</tr>
<tr>
<td>17</td>
<td>Columbus, Ohio, USA</td>
<td>February 1983 to January 1984</td>
<td>229</td>
<td>30 (26)</td>
<td>13 (12)</td>
<td>3 (2.5)</td>
<td>5 (4)</td>
<td>4 (3.5)</td>
<td>–</td>
<td>8 (7)</td>
</tr>
<tr>
<td>18*</td>
<td>Oulu, Finland</td>
<td>May 1986 to May 1987</td>
<td>125</td>
<td>69 (55)</td>
<td>14 (11)</td>
<td>–</td>
<td>–</td>
<td>6 (5)</td>
<td>54 (43)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>19*</td>
<td>Umea, Sweden</td>
<td>December 1982 to November 1984</td>
<td>125</td>
<td>69 (32)</td>
<td>8 (4)</td>
<td>3 (1.5)</td>
<td>3 (1.5)</td>
<td>13 (6.6)</td>
<td>–</td>
<td>1 (0.5)</td>
</tr>
<tr>
<td>20</td>
<td>Baltimore, USA</td>
<td>November 1991 to November 1991</td>
<td>385</td>
<td>69 (17.9)</td>
<td>28 (7.3)</td>
<td>14 (3.6)</td>
<td>13 (3.4)</td>
<td>3 (0.8)</td>
<td>14 (3.6)</td>
<td>26 (6.8)</td>
</tr>
<tr>
<td>21*</td>
<td>Southern Israel, Israel</td>
<td>November 1991 to November 1992</td>
<td>346</td>
<td>148 (42.8)</td>
<td>19 (5.5)</td>
<td>–</td>
<td>–</td>
<td>101 (29.2)</td>
<td>62 (17.9)</td>
<td>–</td>
</tr>
<tr>
<td>11</td>
<td>Ohio, USA</td>
<td>1991</td>
<td>2776</td>
<td>351 (12.6)</td>
<td>184 (6.6)</td>
<td>94 (3.4)</td>
<td>–</td>
<td>404/1244 (32.5)</td>
<td>172/1923 (8.9)</td>
<td>124 (4.5)</td>
</tr>
<tr>
<td>22</td>
<td>Leiden, Netherlands</td>
<td>1985</td>
<td>334</td>
<td>90 (27)</td>
<td>26 (8)</td>
<td>4 (1)</td>
<td>8 (2)</td>
<td>19 (6)</td>
<td>–</td>
<td>11 (3.2)</td>
</tr>
<tr>
<td>23</td>
<td>Arkansas, USA</td>
<td>1985</td>
<td>154</td>
<td>8 (5)</td>
<td>2 (1)</td>
<td>7 (5)</td>
<td>6 (4)</td>
<td>3 (2)</td>
<td>8 (5)</td>
<td>7 (5)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
<td>5379</td>
<td>935 (17.3)</td>
<td>359 (6.6)</td>
<td>159 (2.9)</td>
<td>70 (1.3)</td>
<td>598/4361 (13.7)</td>
<td>332/3292 (10.1)</td>
<td>218 (4.05)</td>
</tr>
</tbody>
</table>

*Serological tests for Streptococcus pneumoniae (usually antibodies to pneumolysin or pneumolysin complexes) used to diagnose pneumococcal pneumonia in addition to blood and, in some cases, sputum culture. AGNR Aerobic Gram-negative rods (such as Escherichia coli, etc); C pneumonia Chlamydia pneumoniae; H influen Haemophilus influenzae; L pneum Legionella pneumophila; M pneum Mycoplasma pneumoniae; S aureus Staphylococcus aureus.
Pneumonia treated on an ambulatory basis: *M pneumoniae* accounts for 17% to 37% of patients with pneumonia treated on an ambulatory basis. Table 1 gives a summary of the studies that have examined the etiology of pneumonia in outpatients (12-15). It is likely that *S pneumoniae* is underdiagnosed in this setting.

CAP requiring admission to hospital: Table 2 gives detailed information on 10 studies of CAP requiring hospitalization (10,11,16-23). *S pneumoniae* is the most commonly implicated agent and accounts for about one-half of all cases of CAP requiring admission to hospital. The second most commonly implicated agent is *C pneumoniae* and the third is *H influenzae*. *L pneumophila* accounts for 2% to 6% of cases of CAP requiring hospitalization. Aerobic Gram-negative bacilli, such as *Escherichia coli* and *Klebsiella* species, are uncommon causes of CAP but are important considerations in patients who require admission to an intensive care unit (ICU). *Mycobacterium tuberculosis* must always be considered as a potential cause of CAP.

Nursing home-acquired pneumonia: Data from six studies of nursing home-acquired pneumonia are presented in Table 3. *S pneumoniae* is the most commonly isolated organism; however, aerobic Gram-negative bacilli such as *Klebsiella* species are commonly isolated from sputum of these patients. The problem is distinguishing colonization from infection.

Pneumonia in patients with chronic obstructive pulmonary disease: *S pneumoniae*, *H influenzae*, *Legionella* species and viridans streptococci were most commonly implicated in one study (29).

Severe CAP: A number of pathogens may be responsible for severe infection requiring treatment in an ICU (Table 4). Initial treatment must, at the least, cover *S pneumoniae*, *Legionella* species, *H influenzae* and aerobic Gram-negative bacilli.

### Table 3

**Etiology of nursing home-acquired pneumonia**

<table>
<thead>
<tr>
<th>Reference</th>
<th>N</th>
<th><em>S pneum</em></th>
<th><em>C pneum</em></th>
<th><em>H influen</em></th>
<th><em>S aureus</em></th>
<th><em>M catarr</em></th>
<th><em>K pneum</em></th>
<th>Other</th>
<th>Aspiration</th>
<th>Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>24</td>
<td>35</td>
<td>9 (26)</td>
<td>2 (6)</td>
<td>9 (26)</td>
<td>14 (40)</td>
<td></td>
<td>7 (5.3)</td>
<td></td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>10</td>
<td>131</td>
<td>9 (6.8)</td>
<td>1 (0.8)</td>
<td>7 (5.3)</td>
<td></td>
<td>7 (5.3)</td>
<td>19 (14.5)</td>
<td>77 (59)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>25</td>
<td>104</td>
<td>31 (29.8)</td>
<td>20 (19)</td>
<td>11 (10.5)</td>
<td>4 (3.8)</td>
<td>24 (23)</td>
<td></td>
<td></td>
<td>14 (13)</td>
<td></td>
</tr>
<tr>
<td>26</td>
<td>56</td>
<td>5 (8.9)</td>
<td>4 (7.1)</td>
<td>1 (1.8)</td>
<td>3 (5.5)</td>
<td>43 (77)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>27</td>
<td>115</td>
<td>7 (6)</td>
<td>3 (2.5)</td>
<td>2 (1.7)</td>
<td>7 (16)</td>
<td>20 (17)</td>
<td>83 (72.8)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>28*</td>
<td>30</td>
<td>2 (6.6)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>23 (76.7)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>471</td>
<td>30 (6.4)</td>
<td>30 (6.4)</td>
<td>7 (1.5)</td>
<td>21 (4.4)</td>
<td>51 (10.8)</td>
<td>240 (51)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

95% CI 1.2 to 29.7 –1.9 to 15 –3.5 to 21 –13.6 to 85

*Serological study – Chlamydia pneumoniae and respiratory syncytial virus-1 and parainfluenza virus 3-1, and influenza virus type A-1, and one each of parainfluenza virus type 3 and influenza virus type A. AGNRs: Aerobic Gram-negative rods; *H influen* Haemophilus influenzae; *K pneum* Klebsiella pneumoniae; *M catarr* Moraxella catarrhalis; *S aureus* Staphylococcus aureus; *S pneum* Streptococcus pneumoniae

### Table 4

**Etiology of community-acquired pneumonia requiring admission to an intensive care unit (ICU)**

<table>
<thead>
<tr>
<th>Reference</th>
<th>Location</th>
<th>Date</th>
<th>N</th>
<th><em>S pneum</em></th>
<th><em>L pneum</em></th>
<th>AGNRs</th>
<th><em>S aureus</em></th>
<th>Unknown</th>
<th>Ventilated</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>30</td>
<td>Spain</td>
<td>1988 to 1990</td>
<td>58</td>
<td>13 (37)</td>
<td>8 (22.8)</td>
<td>4 (11.4)</td>
<td>39.6%</td>
<td>72%</td>
<td>22.4%</td>
<td></td>
</tr>
<tr>
<td>31</td>
<td>United Kingdom (25 hospitals)</td>
<td>1987</td>
<td>60</td>
<td>11 (18)</td>
<td>7 (12)</td>
<td>2 (3)</td>
<td>30%</td>
<td>88%</td>
<td>48%</td>
<td></td>
</tr>
<tr>
<td>32*</td>
<td>France</td>
<td>1987 to 1989</td>
<td>132</td>
<td>43 (32)</td>
<td>4 (3)</td>
<td>14 (11)</td>
<td>5 (4)</td>
<td>28%</td>
<td>37%</td>
<td>24%</td>
</tr>
<tr>
<td>33</td>
<td>Spain (26 ICUs)</td>
<td>1991 to 1992</td>
<td>262</td>
<td>30 (11)</td>
<td>21 (8)</td>
<td>8 (3)</td>
<td>10 (4)</td>
<td>41.2%</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>34</td>
<td>Sweden</td>
<td>1977 to 1981</td>
<td>53</td>
<td>15 (28)</td>
<td></td>
<td>2 (4)</td>
<td>25%</td>
<td>58%</td>
<td>25%</td>
<td></td>
</tr>
<tr>
<td>35</td>
<td>Seville, Spain</td>
<td>1985 to 1987</td>
<td>67</td>
<td>12 (37.5)</td>
<td>7 (21.8)</td>
<td>8 (25)</td>
<td>52.3%</td>
<td>20.8%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>36*</td>
<td>Barcelona, Spain</td>
<td>1984 to 1987</td>
<td>92</td>
<td>13 (14)</td>
<td>13 (14)</td>
<td>5 (5)</td>
<td>30%</td>
<td>61%</td>
<td>20%</td>
<td></td>
</tr>
<tr>
<td>37</td>
<td>Lille, France</td>
<td>1987 to 1991</td>
<td>299</td>
<td>80 (26.7)</td>
<td>52 (17.3)</td>
<td>57 (Staph species) (18)</td>
<td>34.1%</td>
<td>50%</td>
<td>28.5%</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td>1023</td>
<td>217 (21)</td>
<td>60 (5.8)</td>
<td>91 (8.8)</td>
<td>76 (7.4)</td>
<td>35%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

95% CI 1.2 to 29.7 –1.9 to 15 –3.5 to 21 –13.6 to 42.9

*Immunosuppressed patients excluded; †Five patients with Pseudomonas aeruginosa had bronchiectasis. AGNRs: Aerobic Gram-negative rods; *L pneum* Legionella pneumophila; NS Not stated; *S aureus* Staphylococcus aureus; *S pneum* Streptococcus pneumoniae; Staphylococcus
Poly microbial infection: The issue of microbial etiology of CAP is further complicated by the fact that doctors now realize that more than one pathogen may be responsible for disease in any given patient. Such mixed infections are well known in hospital-acquired pneumonia, and in one study (38), it was shown that multiple pathogens were present in over one-half of the patients studied. In CAP, the incidence of mixed infections appears to be lower, ranging from 2.7% to 10% in the studies of patients requiring admission to hospital (16,39,40).

DIAGNOSIS

The subject of diagnostic testing of patients with CAP has generated considerable debate among pulmonologists and infectious disease specialists. The recommendations have ranged from the limited testing recommended by the ATS guidelines and the European Study on CAP (ESOCA P) Committee to the more extensive testing recommended by the IDSA (2,3,41).

There are many advantages to determining a specific etiological agent including selecting the optimal drug to deal with the offending pathogen(s); reducing antibiotic abuse in terms of cost, resistance and adverse drug reactions; and identifying organisms that have potential epidemiological significance such as M tuberculosis, Legionella species and drug-resistant S pneumoniae. Unfortunately, the reality of current clinical practice is that, despite extensive diagnostic testing even in medical centres interested in the epidemiology of pneumonia, a specific etiological agent will not be found in one-third to one-half of cases (10,16). With the possible exception of a sputum Gram stain, the information obtained comes at a time when the most significant decisions regarding antimicrobial therapy have already been made. Although studies assessing the direct impact of diagnostic testing on clinical outcomes have not been performed, a body of evidence is emerging to suggest that knowledge of the pathogen may not affect the clinical outcome (35). Antibiotics found to be initially effective against the target pathogen are associated with better outcomes, but the identification of that target pathogen has no beneficial effect on outcome (42). Identification of the organism after the initial incorrect choice of empirical therapy and subsequent correction of therapy to cover the offending pathogen does not appear to affect outcome (37). Woodhead and colleagues (43) found that in routine clinical practice (as opposed to carefully conducted prospective diagnostic investigations), causative pathogens are found in approximately 25% of cases, but the results of these investigations change therapy in less than 10% of cases. They concluded that routine microbial investigation of all adults admitted to hospital was not helpful and was probably unnecessary.

The authors of the current Canadian document have made recommendations for investigations based upon the severity of illness of the patient. This is reflected in the site of care selected by the physician and, accordingly, these recommendations will be site specific. Recommendations for patients deemed well enough to be treated on an ambulatory basis are different from those for patients ill enough to require hospitalization, either in a general ward or an ICU.
These tests be performed routinely in all patients referred to the prospectively for mortality risk. The panel recommends that operated by Fine and co-workers (49), and they have been validated significant abnormalities of these laboratory tests have been saturation are recommended (level II evidence) (Figure 1). Sign-
studies, renal function studies and an assessment of oxygen assessment based on the initial clinical and radiographical find-
ings, a complete blood count, electrolytes, liver function studies, renal function studies and an assessment of oxygen saturation are recommended (level II evidence) (Figure 1). Significant abnormalities of these laboratory tests have been identified as risk factors for a complicated hospital course or mortality. They have been used in the prediction rule developed by Fine and co-workers (49), and they have been validated prospectively for mortality risk. The panel recommends that these tests be performed routinely in all patients referred to the emergency department to help assess the severity of illness (level II evidence). Although this score can be used to evaluate mortality risk, it has not been validated as a predictor of hospital admission. There is no evidence to suggest that these investigations are useful in the routine assessment of patients in any other clinical setting (physician’s office or nursing home). The panel recommends that arterial blood gases be considered for patients with COPD because oxygen saturation assessment will not inform the physician of hypercapnic respiratory failure (level III evidence). If patients do not have specific risk factors for a complicated course or mortality, and there are no other reasons for admission, the physician will in all likelihood select empirical therapy and discharge the patient from the emergency department.

Laboratory assessment: Unless clinical or radiographical findings suggest risk factors for a poor outcome, the routine laboratory assessment of ambulatory patients suspected of having CAP is unnecessary (level III evidence). Once a patient has been directed to the emergency department for further assessment based on the initial clinical and radiographical findings, a complete blood count, electrolytes, liver function studies, renal function studies and an assessment of oxygen saturation are recommended (level II evidence) (Figure 1). Significant abnormalities of these laboratory tests have been identified as risk factors for a complicated hospital course or mortality. They have been used in the prediction rule developed by Fine and co-workers (49), and they have been validated prospectively for mortality risk. The panel recommends that these tests be performed routinely in all patients referred to the emergency department to help assess the severity of illness (level II evidence). Although this score can be used to evaluate mortality risk, it has not been validated as a predictor of hospital admission. There is no evidence to suggest that these investigations are useful in the routine assessment of patients in any other clinical setting (physician’s office or nursing home). The panel recommends that arterial blood gases be considered for patients with COPD because oxygen saturation assessment will not inform the physician of hypercapnic respiratory failure (level III evidence). If patients do not have specific risk factors for a complicated course or mortality, and there are no other reasons for admission, the physician will in all likelihood select empirical therapy and discharge the patient from the emergency department.

Microbiological assessment
Sputum Gram stain and culture: For the majority of patients treated on an outpatient basis, no specific microbiological investigations are recommended (level II evidence). Direct staining of sputum may be diagnostic for infections caused by *Mycobacterium* species, *Legionella* species, *Pneumocystis carinii* and endemic fungi. Clinical circumstances should dictate the use of these tests for individual patients (risk of exposure, residence in an endemic area, compatible clinical picture). Suspic-
pion of possible pneumococcal infection based on the results of the Gram stain as a rapid diagnostic tool may be particularly helpful in regions where significant pneumococcal resistance is problematic, and where the initial empirical therapeutic choices may change. For patients admitted to the hospital ward, the panel recommends that sputum Gram stain and culture be obtained if an adequate sample (less than 25 squa-
mous epithelial cells/low power field on cytological screening, rapid assessment within 1 to 2 h of production of the sample, properly trained staff to interpret the results) can be obtained before administration of an antibiotic (level II evidence). Ther-

apy should not be delayed in acutely ill patients if there is diffi-
culty obtaining an adequate specimen. Given these constraints, it seems likely that many admitted patients will be started on empirical therapy without the benefit of a sputum Gram stain or culture. For patients admitted to the ICU, a more concerted effort to obtain lower respiratory tract secretions is recommended (level III evidence). Because these patients are monitored closely and may be intubated, it is more likely that an interpretable sample will be obtained.

A review of the extensive literature on sputum Gram stain has indicated that the test is neither sensitive nor specific for the diagnosis of etiological agent in patients with CAP (50). There is considerable inter- and intraobserver variability in the interpretation of the Gram stain results (51). Most of the studies examining the role of this test have depended upon sputum culture as the reference standard. Sputum culture is notorious for its poor test characteristics and, thus, using it to judge the quality of a Gram stain is problematic at best and misleading at worst. The routine use of sputum Gram stain, therefore, cannot be recommended (level II evidence). Routine sputum culture is neither sensitive nor specific. Among patients with pneumococcal pneumonia verified using reliable sources (blood culture, transtracheal aspirate, bronchoalveolar lavage), simultaneous sputum cultures are positive in only 50% of pa-
tients (52). Particularly in patients with COPD but in other pa-
tients as well, false-positive cultures related to chronic coloni-
zation render the interpretation of sputum cultures problematic at best in most situations.

Blood cultures: The panel recommends that two blood cul-
tures be obtained from all hospitalized patients (level II evi-
dence). Bacteremia is present in 6.6% to 17.6% of all hospital-
ized patients with CAP. Although patients with HIV are predisposed to pneumococcal pneumonia, pneumococcal bac-
teria is not more common in HIV-infected individuals than in noninfected patients (39). The incidence of bacteremia in ambulatory patients with CAP is lower, but the precise figure is unknown (53). Among patients admitted to the ICU with CAP, the incidence of bacteremia is higher, ranging from 10.3% to 27%. The administration of antibiotics before hospital admis-
sion reduces the diagnostic yield of blood cultures. Among pa-
tients with bacteremia, the most common pathogen is *S. pneumoniae*, and pneumococcal pneumonia is complicated by bacteremia more frequently than pneumonia caused by other organisms. Although bacteremic patients have a higher mor-
tality than do nonbacteremic patients, this may reflect host factors and severity of illness rather than the bacteremia itself. The exception to this may be among patients with recurrent bact-
teria or those who are HIV-positive.

Thoracentesis: The panel recommends diagnostic thoracentesi-
sis in any patient suspected of CAP with a significant pleural fluid collection (greater than 10 mm in thickness on the lateral decubitus radiographical view) (54) (level II evidence). The incidence of pleural effusion associated with pneumonia ranges from 36% to 57%, and is most common in patients with pneumococcal pneumonia (55). Patients presenting later in the course of their pneumonia and those who are bacteremic are more likely to have a parapneumonic effusion (56). Anaerobes
are the most common cause of frank empyema, occurring either alone or in conjunction with aerobes (57). Patients with pneumococcal pneumonia and parapneumonic effusions, even with positive pleural fluid bacteriology, show a relatively good response to antimicrobial therapy and may not require drainage (54).

**Serology:** The panel recommends that serology not be performed as part of the routine management of patients with CAP (level II evidence). These tests are usually not helpful in the early management of CAP patients because the results of acute and convalescent titres are required before ascribing clinical illness to these pathogens. Cold agglutinins are neither sensitive nor specific to detect infection with *M pneumoniae* and are not recommended (58) (level II evidence). Serological response to *Mycoplasma, Chlamydia* and *Legionella* species usually takes weeks to develop after symptoms occur, reducing the value of these investigations except for epidemiological purposes.

**Legionella urinary antigen:** The panel recommends the *Legionella* species urinary antigen test as part of the routine management of patients with severe CAP, especially those admitted to the ICU (level II evidence). This test identifies only *L pneumophila* serogroup 1, which is the most common serogroup causing clinical illness. The test has a sensitivity of 70% and a specificity of 100%, and is easily and rapidly performed (59). A negative urinary antigen test does not exclude the diagnosis, particularly if it is caused by organisms other than *L pneumophila* serogroup 1, but a positive test is diagnostic of infection.

**DNA probes and amplification:** DNA probes and amplification tools are being rapidly developed to assist clinicians with the rapid and accurate diagnosis of problem pathogens such as *C pneumoniae* or *M pneumoniae*. These organisms can be rapidly identified from a single throat swab (60). However, the role of these new tests is under investigation, and recommendations cannot be made until their test properties have been clarified.

**Invasive procedures:** The panel does not recommend the routine use of invasive testing in patients suspected of having CAP (level II evidence). There may, however, be circumstances when bronchoscopy, bronchoalveolar lavage, protected specimen brush or percutaneous lung needle aspiration may be useful, such as in patients with fulminant pneumonia or those unresponsive to a standard course of antimicrobial therapy (61).

**Summary:** The panel recommends few investigations as part of the routine management of patients with CAP, especially those treated on an ambulatory basis. As the severity of illness increases and the risk factors for a complicated course or mortality increase, the panel recommends more intense investigations. Microbiological investigations are warranted for patients requiring admission to hospital if rapid access to competent microbiological services is available, particularly if there is a clinical suspicion of infection with unusual organisms such as *M tuberculosis* or endemic fungi. Further studies are required to recommend more precisely the role of new technologies devised to assist in the diagnosis of specific etiological agents.

**TREATMENT**

The previous Canadian and ATS CAP guidelines focused on treatment recommendations based on the presence or absence of comorbid conditions, severity of illness upon clinical presentation, and whether treatment was to be given on an outpatient or inpatient basis (1,2). These guidelines were well received because they provided the practicing physician with a rational and manageable approach to the initial selection of antimicrobials for the empirical treatment of this common condition. However, a number of important developments that significantly affect our decisions regarding the management of CAP have transpired since the publication of these earlier guidelines. First, the landmark studies of Fine et al (49,62,63) have provided a sound basis for mortality risk prediction and decisions concerning hospital admission or discharge. This, in turn, has allowed improved judgment in choosing the initial site of care for patients and the development of critical pathways for the management of CAP in the institutional setting (64-66). Second, the increasing prevalence of antimicrobial resistance in common lower respiratory tract pathogens has meant that antimicrobial agents previously considered as first-line must be re-evaluated. Third, the availability of new macrolides and ‘respiratory’ fluoroquinolones with improved in vitro activity and pharmacokinetic/pharmacodynamic properties has necessitated a reassessment of both the choice and mode of administration of antimicrobial agents during initial management. On the other hand, the potential for the rapid development of resistance to these agents, *S pneumoniae* in particular, and the recognition of serious toxicity associated with some of the newer fluoroquinolones have raised major concerns regarding the indiscriminate use of these agents. Finally, the ability to administer many agents once daily either orally, intravenously or sequentially from an intravenous to oral route, as well as the ready access to home intravenous antibiotic programs and home nursing visits, has greatly reduced the need for and duration of hospitalization of many patients with CAP.

The following update for the initial management of CAP is recommended by the consensus group. These treatment guidelines are stratified according to the site of care of the patient, ie, outpatient, nursing home resident, hospitalized patient on a general medical ward or hospitalized patient in an ICU. To make the current guidelines useful to practicing physicians, a major effort has been made to simplify the recommendations as much as possible to emphasize the general principles applicable to the majority of patients with CAP. Accordingly, recommendations for the initial empirical management of CAP are predicated on the most likely pathogens in a given population, the general trend of antibiotic resistance among respiratory pathogens locally and across Canada, and the clinical experience of these antibiotic regimens based on randomized, controlled trials. Rather than attempting to address all the possible factors that may be of dubious significance or difficult to document in a given patient, only the most important modifying factors are considered. These factors either affect oropharyngeal colonization by more resistant Gram-negative pathogens or may result in antimicrobial pressure imposed by previous antibiotic therapy. In addition, unique features of the healthcare delivery system within Canada such as the infrastructure support of its healthcare institutions including nurs-
ing homes, the availability and cost of intravenous and oral antibiotics in general, and the relative inaccessibility to parenteral antibiotics in the nursing home setting were taken into consideration.

**Site-specific initial antimicrobial treatment of CAP:** The authors have continued with the general approach adopted by the previous Canadian guidelines of categorizing patients into groups of those who can be treated as outpatients, those who are nursing home residents and those who require hospitalization. A detailed discussion of the studies supporting the use of the various regimens suggested here can be found in the extended version of these guidelines (4).

Patients with a pneumonia-specific severity score of greater than 90 according to the criteria of Fine et al (49) should be hospitalized (level I evidence) (Figure 2). Patients with CAP who do not require hospitalization are categorized separately into outpatients and nursing home residents. For outpatients who do not have modifying factors such as COPD or macroaspiration, treatment with a macrolide (erythromycin, azithromycin or clarithromycin) or doxycycline should suffice to treat pneumococci and ‘atypical’ pathogens such as *M pneumoniae* and *C pneumoniae* (level II evidence) (Table 5). Both macrolides and doxycycline remain effective as monotherapy for patients with mild to moderately severe CAP based on their pneumonia-specific severity of illness score (Figure 2). Patients with COPD who have not received antibiotics or oral steroids during the previous three months can be treated in an identical fashion as patients without modifying factors with the caveat that only a newer macrolide (azithromycin or clarithromycin) be used to insure adequate coverage of *H influenzae*. Patients with COPD and a history of use of antibiotics or oral steroids within the past three months may have an increased risk of *H influenzae* and enteric Gram-negative bacilli, in addition to *S pneumoniae, C pneumoniae* and *L pneumophila* infection, and a ‘respiratory’ fluoroquinolone is recommended. On the basis of the safety data related to serious liver injury, trovafloxacin should be reserved only for hospitalized patients whose infections are judged to be serious and life-threatening, and when the benefit is believed to outweigh the potential risk. Amoxicillin-clavulanate or a second-generation cephalosporin (eg, cefuroxime or cefprozil), each with or without a macrolide, is considered a second choice (level II evidence). If macroaspiration is suspected, a fourth-generation fluoroquinolone with enhanced activity against anaerobes (eg, moxifloxacin, gatifloxacin) should be considered (level II evidence). Alternatively, a third-generation fluoroquinolone (eg, levofloxacin) plus either clindamycin or metronidazole is appropriate (level III evidence). The choice of initial treatment of CAP for patients with HIV infection is beyond the scope of the current guidelines.

Nursing home residents with pneumonia can be evaluated with the same prediction rules for hospitalization as other patients with CAP (67) (level II evidence) (Table 1). For patients who can be treated in the nursing home setting and do not require hospitalization, a ‘respiratory’ fluoroquinolone or amoxicillin-clavulanate plus a macrolide is recommended as the first choice. A second-generation cephalosporin plus a macrolide is an alternative (68) (level II evidence).

Patients requiring hospitalization, including those transferred from a nursing home, can be divided into those who are managed on a general medical ward and those who require cardioventilatory support in an ICU. Treatment of patients on the general medical ward is directed at bacteremic pneumococcal pneumonia as well as *H influenzae*, enteric Gram-
TABLE 5
Empirical antimicrobial selection for adult patients with community-acquired pneumonia

<table>
<thead>
<tr>
<th>Type of pneumonia</th>
<th>Modifying factors and/or pathogens</th>
<th>First choice</th>
<th>Second choice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outpatient without modifying factors</td>
<td>COPD (no recent antibiotics or oral steroids within past 3 months)</td>
<td>Macrolide*</td>
<td>Doxycycline</td>
</tr>
<tr>
<td>Outpatient with modifying factors</td>
<td>COPD (recent antibiotics or oral steroids within past 3 months) – Haemophilus influenzae and enteric Gram-negative rods</td>
<td>Newer macrolides†</td>
<td>Doxycycline</td>
</tr>
<tr>
<td></td>
<td>Suspected macroaspiration – oral anaerobes</td>
<td>'Respiratory' fluoroquinolone†</td>
<td>Amoxicillin-clavulanate + macrolide or second-generation cephalosporin + macrolide</td>
</tr>
<tr>
<td>Nursing home residents in nursing home</td>
<td>Streptococcus pneumoniae, enteric Gram-negative rods, H influenzae</td>
<td>'Respiratory' fluoroquinolone† alone or amoxicillin-clavulanate + macrolide</td>
<td>Third-generation fluoroquinolones‡ (eg, levofloxacin) plus clindamycin or metronidazole</td>
</tr>
<tr>
<td>Nursing home residents in hospital</td>
<td>S pneumoniae, Legionella pneumophila, Chlamydia pneumoniae</td>
<td>Identical to treatment for other hospitalized patients (see below)</td>
<td>Second-, third- or fourth-generation cephalosporin + macrolide</td>
</tr>
<tr>
<td>Hospitalized patient on medical ward</td>
<td>P aeruginosa not suspected (S pneumoniae, L pneumophila, C pneumoniae, enteric Gram-negative rods)</td>
<td>IV 'respiratory' fluoroquinolone‡ + cefotaxime, ceftriaxone or beta-lactam/beta-lactamase inhibitor</td>
<td>IV macrolide + cefotaxime, ceftriaxone or beta-lactam/beta-lactamase inhibitor</td>
</tr>
<tr>
<td>Hospitalized in intensive care unit</td>
<td>P aeruginosa suspected</td>
<td>Antipseudomonal fluoroquinolone‡ plus antipseudomonal beta-lactam (eg, ciprofloxacin) plus antipseudomonal beta-lactam (eg, ceftazidime, carbapenem, piperacillin-tazobactam, carbapenem) or aminoglycoside (eg, gentamicin, tobramycin, amikacin)</td>
<td>Triple therapy with antipseudomonal beta-lactam plus aminoglycoside plus macrolide</td>
</tr>
</tbody>
</table>

*Macrolide – Erythromycin, azithromycin, clarithromycin; †Newer macrolide – Azithromycin, clarithromycin; ‡Respiratory fluoroquinolone – Levofloxacin (third generation), gatifloxacin and moxifloxacin (fourth generation); trovafloxacin (fourth generation) is restricted because of potential severe hepatotoxicity. COPD Chronic obstructive pulmonary disease; IV Intravenous.

negative bacilli and severe Legionella or Chlamydia species infection. Monotherapy with a ‘respiratory’ fluoroquinolone is the first choice (level II evidence). A second-, third- or fourth-generation cephalosporin (eg, cefuroxime, cefotaxime, ceftriaxone, cefixime or cefepime) plus a macrolide is an alternative treatment. Monotherapy with a fluoroquinolone for hospitalized ward patients offers logistical and financial advantages over combination therapy with a macrolide and a beta-lactam. There are also some data suggesting that use of a fluoroquinolone alone may be associated with a reduction in mortality (69,70).

Choice of treatment for patients in the ICU depends upon whether P aeruginosa is a concern (eg, in patients with severe structural lung disease and patients who have recently completed a course of antibiotics or steroids). If P aeruginosa is not an issue, broad spectrum aggressive coverage is still required in the form of an intravenous macrolide or ‘respiratory’ fluoroquinolone plus a nonpseudomonal third-generation cephalosporin (eg, cefotaxime, ceftriaxone) or a beta-lactam/beta-lactamase inhibitor. If P aeruginosa is suspected, an antipseudomonal fluoroquinolone (eg, ciprofloxacin) plus an antipseudomonal beta-lactam (eg, ceftazidime, piperacillin-tazobactam or carbapenem) or an aminoglycoside (eg, gentamicin, tobramycin or amikacin if antibiotic resistance is not a major concern) should be used (level III evidence). An alternative regimen is triple therapy with an antipseudomonal beta-lactam plus an aminoglycoside plus a macrolide. It should be noted that whereas synergy between an antipseudomonal beta-lactam and an aminoglycoside can frequently be demonstrated for P aeruginosa in vitro, such synergistic interaction is uncommon between a fluoroquinolone and an aminoglycoside (71,72). An additive effect can be expected while antagonism is rare. There are insufficient efficacy data to recommend trovafloxacin, either alone or in combination with an antipseudomonal beta-lactam, as the initial empirical treatment of serious P aeruginosa infections at the present time.

It is important to recognize that these recommendations are derived from a consensus of experts and are not entirely based on evidence from randomized, controlled trials. Once an etiological agent has been appropriately identified, its in vitro susceptibility confirmed and infection with a copathogen excluded, initial empirical therapy should be modified to a narrower focus and directed at the specific pathogen(s) whenever possible (Table 6).

Unfortunately, there has never been an appropriately designed randomized, controlled trial to determine specifically the duration of antibiotic therapy for CAP. Most physicians, including members of this committee, treat for one to two weeks depending upon the clinical response of the patient.
Specific therapy for selected pathogens in community-acquired pneumonia (CAP)

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Streptococcus pneumoniae</td>
<td></td>
</tr>
<tr>
<td>Penicillin sensitive (MIC &lt; 0.1 mg/L)</td>
<td>Oral penicillin G, amoxicillin, cephalexin, clindamycin or macrolide</td>
</tr>
<tr>
<td>Intermediate resistance (MIC 0.1 to 1 mg/L)</td>
<td>Aminoglycoside, amoxicillin, cefuroxime (500 mg bid PO)</td>
</tr>
<tr>
<td>High level resistance (MIC &gt; 1 mg/L)</td>
<td>Penicillin G (2 MU every 6 h IV), cefotaxime (1 g every 8 h IV), or ceftriaxone (1 g every 24 h IV), or ‘respiratory’ fluoroquinolone*</td>
</tr>
<tr>
<td>CAP with high level resistance and associated meningitis</td>
<td>Vancomycin or ‘respiratory’ fluoroquinolone*</td>
</tr>
<tr>
<td>Haemophilus influenzae</td>
<td>Cephalosporin (second or third generation) or beta-lactam/beta-lactamase inhibitor</td>
</tr>
<tr>
<td>Moraxella catarrhalis</td>
<td>Cefepime (second or third generation) or beta-lactam/beta-lactamase inhibitor</td>
</tr>
<tr>
<td>Respiratory anaerobes</td>
<td>Beta-lactam/beta-lactamase inhibitor or third-generation fluoroquinolone (eg, levofloxacin) + either clindamycin or metronidazole, or fourth-generation fluoroquinolone (eg, moxifloxacin)</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td></td>
</tr>
<tr>
<td>Methicillin-sensitive</td>
<td>Oxacillin or cloxacillin</td>
</tr>
<tr>
<td>Methicillin-resistant</td>
<td>Vancomycin</td>
</tr>
<tr>
<td>Enteric Gram-negative bacilli</td>
<td>Cephalosporin (third or fourth generation) + aminoglycoside</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>Ciprofloxacin or amikacin, each + antipseudomonal beta-lactam†</td>
</tr>
<tr>
<td>Legionella species</td>
<td>Macrolide + rifampin or fluoroquinolone</td>
</tr>
<tr>
<td>Chlamydia pneumoniae</td>
<td>Doxycycline or macrolide</td>
</tr>
<tr>
<td>Mycoplasma pneumoniae</td>
<td>Doxycycline or macrolide</td>
</tr>
<tr>
<td>Coxiella burnetti (Q fever)</td>
<td>Tetracycline</td>
</tr>
</tbody>
</table>

*levofloxacin or trovafloxacin; †Cefotaxime, piperacillin-tazobactam, imipenem or meropenem. IV Intravenous; MIC Minimal inhibitory concentration; MU Million units; PO Orally

Assessment of the response to initial treatment: The rate of clinical response of patients with CAP to antimicrobial therapy depends on the pathogen as well as host factors (73). However, a subjective response is usually noted within three days of initiating treatment. Objective parameters are the resolution of respiratory symptoms (cough or dyspnea), defervescence of fever, improvement in the arterial partial pressure of oxygen and serial chest radiographs, and normalization of the leukocyte count. The length of hospital stay is often determined by the duration of intravenous antimicrobial regimens. IntraVenous to oral sequential therapy is strongly recommended because it reduces the cost and shortens the length of hospital stay, and provides additional psychosocial benefit for the patient (level I evidence).

Patients who fail to respond to treatment despite what appears to be an appropriate choice of antimicrobial therapy should be re-evaluated at three to five days after the initiation of treatment. Possible reasons for failure include complicated pneumonia such as the presence of an empyema, bronchial obstruction or extrapulmonary spread of infection, superinfection or misdiagnosis of noninfectious causes (eg, congestive heart failure, neoplasm, vasculitis, sarcoidosis, drug reaction, alveolitis, pulmonary embolism or hemorrhage). Additional diagnostic procedures such as CT scan, bronchoscopy, mediastinoscopy, angiography or lung biopsy may be required.

General measures and follow-up: In addition to antimicrobial therapy, certain general principles of management should be implemented. Adequate hydration will help to clear secretions. Cough suppressants may be beneficial in patients with severe paroxysms of coughing that produce respiratory fatigue or pleuritic and chest wall pain. Oxygen therapy is indicated for hypoxemia. Significant pleural effusion (greater than 10 mm on lateral decubitus) or pleural empyema should be drained either by needle aspiration under CT guidance or surgically. Patients treated in the outpatient setting must be carefully monitored to ensure compliance and clinical improvement. Follow-up of the patient by telephone or a return clinic visit within 48 to 72 h is strongly suggested. Additional visits and a repeat chest x-ray within two to three weeks of antimicrobial therapy may be beneficial to ensure the resolution of the pneumonia.

Prevention of CAP: The importance of pneumococcal infection in CAP is apparent, but it is also clear that during outbreaks of influenza, the influenza virus has a significant impact on CAP as well. Both of these infections may be prevented by the use of pneumococcal and influenza vaccines, respectively. The former is a polyvalent preparation containing purified capsular polysaccharide of the serotypes responsible for most of the invasive pneumococcal infections. The latter vaccine is altered on a yearly basis to contain antigens of the influenza strains that are anticipated to cause problems in the coming season.

A detailed discussion of these vaccines is beyond the scope of this document, but the interested reader is referred to the following papers for additional information (74-77). The committee supports the use of the currently available pneumococcal (level II) and influenza (level I) vaccines in unvaccinated patients at risk for infection with either of these pathogens, or in those at increased risk of complications from such infections.
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