Pneumonia Due to *Pseudomonas aeruginosa*

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Recent Advances in Chest Medicine

**Pneumonia Due to *Pseudomonas aeruginosa***

Part I: Epidemiology, Clinical Diagnosis, and Source

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Pseudomonas aeruginosa is an uncommon cause of community-acquired pneumonia (CAP), but a common cause of hospital-acquired pneumonia. Controversies exist for diagnostic methods and antibiotic therapy. We review the epidemiology of CAP, including that in patients with HIV and also in hospital-acquired pneumonia, including ventilator-associated pneumonia (VAP) and bronchoscope-associated pneumonia. We performed a literature review of clinical studies involving *P aeruginosa* pneumonia with an emphasis on treatment and prevention. Pneumonia due to *P aeruginosa* occurs in several distinct syndromes: (1) CAP, usually in patients with chronic lung disease; (2) hospital-acquired pneumonia, usually occurring in the ICU; and (3) bacteremic *P aeruginosa* pneumonia, usually in the neutropenic host. Radiologic manifestations are nonspecific. Colonization with *P aeruginosa* in COPD and in hospitalized patients is a well established phenomenon such that treatment based on respiratory tract cultures may lead to overtreatment. We present circumstantial evidence that the incidence of *P aeruginosa* has been overestimated for hospital-acquired pneumonia and reflex administration of empirical antipseudomonal antibiotic therapy may be unnecessary. A diagnostic approach with BAL and protected specimen brush using quantitative cultures for patients with VAP led to a decrease in broad-spectrum antibiotic use and improved outcome. Endotracheal aspirate cultures with quantitative counts are commonly used, but validation is lacking. An empirical approach using the Clinical Pulmonary Infection Score is a pragmatic approach that minimizes antibiotic resistance and leads to decreased mortality in patients in the ICU. The source of the *P aeruginosa* may be endogenous (from respiratory or GI tract colonization) or exogenous from tap water in hospital-acquired pneumonia. The latter source is amenable to preventive measures.
Abbreviations

CAP
    community-acquired pneumonia

CPIS
    Clinical Pulmonary Infection Score

HAART
    highly active antiretroviral therapy

VAP
    ventilator-associated pneumonia

*Pseudomonas aeruginosa* is a gram-negative rod that is ubiquitous in nature and an opportunistic pathogen in humans. *P aeruginosa* is a particularly virulent pathogen that produces many virulence factors, including exotoxins and enzymes. It also produces a biofilm that protects it from environmental elements and from host antibodies and phagocytes. We initiated a review of pneumonias caused by *P aeruginosa* given its apparent increase in incidence and new challenges in treatment. *P aeruginosa* pneumonia occurring in patients with cystic fibrosis is a distinct entity linked to an underlying airway disorder and is beyond the scope of this review.

**Historical Overview**

Among the anatomic sites of *P aeruginosa* infection, the lung is associated with the highest mortality rate. The classic features of pneumonia due to *P aeruginosa* are its occurrence in a compromised host with hemorrhagic and necrotizing lung pathology. Respiratory infections due to *P aeruginosa* were reported in the late 19th century but were exceedingly rare. The pathologic features of bacteremic *P aeruginosa* pneumonia were described as early as 1917 and were characterized by blood vessel invasion and necrosis. Nonbacteremic *P aeruginosa* pneumonia was characterized by microabscesses, hemorrhage, and focal necrosis.

Several distinct syndromes of *P aeruginosa* respiratory tract infection are relevant to the clinician. The first is community-acquired pneumonia (CAP), in which *P aeruginosa* colonization in the upper airway leads to infection of the lung. This is presumably the mechanism for pneumonia in children with cystic fibrosis and patients with chronic lung disease. *P aeruginosa* pneumonia associated with bronchiectasis is now rare. A second, more common syndrome is associated with an ICU pneumonia with (1) aspiration from contaminated nebulizer fluid or from mechanical ventilation, or (2) hospital-acquired pneumonia in the setting of preexisting colonization in patients with chronic lung disease. The third syndrome is *P aeruginosa* bacteremia in the immunosuppressed host, usually with neutropenia, in which the lung is infected by hematogenous dissemination. From a therapeutic perspective, these distinctions are important because the superior efficacy of combination antibiotic therapy was first reported primarily in bacteremic patients with hematologic malignancy.

**Epidemiology**

**Hospital-Acquired Pneumonia**

In the late 1980s, the Centers for Disease Control National Nosocomial Infection Study noted the gradual increase in incidence of *P aeruginosa* pneumonia as a hospital-acquired pathogen. From 1975 to 2003, the incidence of hospital-acquired pneumonia caused by *P aeruginosa* has almost doubled, from 9.6% to 18.1%. In a national large-scale survey of US ICUs, *P aeruginosa* was the most frequently isolated gram-negative aerobic bacterium from ICUs (23%, 8,244/35,790) and also the most frequent bacterium isolated from the respiratory tract (31.6%). At the University of Pittsburgh, *P aeruginosa* was the most frequent cause (20%) of 670 cases of ventilator-associated pneumonia (VAP) as diagnosed by isolation from mini-BAL and bronchoscopic procedures. In a retrospective matched cohort study of 842 patients with VAP in the United States, *P aeruginosa* was the most frequent pathogen isolated (9.3%) in patients with VAP in which pneumonia occurred > 4 days after the start of mechanical ventilation.

VAP caused by *P aeruginosa* is associated with a high crude mortality of 42.1% to 87% and a high attributable mortality of 32% to 42.8%, even among patients receiving appropriate antimicrobial therapy (Table 1). An economic analysis assessed the financial impact of an outbreak of *P aeruginosa*
infections in a 27-bed ICU in Spain. Seventeen patients were involved and almost all had *P. aeruginosa* respiratory tract infection: Mortality was 47%. A conservative estimate of extra cost attributable to *P. aeruginosa* infection was US $421,000, which included diagnostic procedures, pharmacy costs, and ICU stay. The mean cost for each case of *P. aeruginosa* infection was US $24,700 over a median 45 days of hospitalization.\[22\]

**Table 1 -- Crude and Attributable Mortality of Ventilator-Associated Pneumonia Caused by *P. aeruginosa***

<table>
<thead>
<tr>
<th>Study/Year</th>
<th>No. of <em>P. aeruginosa</em></th>
<th>Crude Mortality, %</th>
<th>Attributable Mortality, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Garnacho-Montero et al[17]/2007</td>
<td>183</td>
<td>42.1</td>
<td>NA</td>
</tr>
<tr>
<td>Zavascki et al[21]/2006</td>
<td>55</td>
<td>60</td>
<td>NA</td>
</tr>
<tr>
<td>Trouillet et al[20]/2002</td>
<td>135</td>
<td>51.9</td>
<td>NA</td>
</tr>
<tr>
<td>Ibrahim et al[18]/2001</td>
<td>49</td>
<td>51</td>
<td>NA</td>
</tr>
<tr>
<td>Crouch Brewer et al[14]/1996</td>
<td>38</td>
<td>69</td>
<td>38</td>
</tr>
<tr>
<td>Kollef et al[19]/1995</td>
<td>20 (P. aeruginosa = 16)</td>
<td>65</td>
<td>34</td>
</tr>
<tr>
<td>Fagon et al[15]/1993</td>
<td>21</td>
<td>71.4</td>
<td>42.8</td>
</tr>
<tr>
<td>Fagon et al[16]/1989</td>
<td>16</td>
<td>87</td>
<td>32</td>
</tr>
</tbody>
</table>

NA = not available; *P. aeruginosa* = *Pseudomonas aeruginosa*.

**Bronchoscope-Associated *P. aeruginosa* Pneumonia**

Hospital-acquired pneumonia by *P. aeruginosa* may also be iatrogenic. In several investigations, the source of the *P. aeruginosa* was found to be contaminated bronchoscopes. Isolates of *P. aeruginosa* from the environment, the bronchoscope, and the patient undergoing this procedure have been linked by various subtyping methods (Table 2 \[23\], \[24\], \[25\], \[26\], \[27\], \[28\], \[29\], \[30\], \[31\], \[32\], \[33\]).

**Table 2 -- Reports of Bronchoscope-Associated Pneumonia Due to *P. aeruginosa***

<table>
<thead>
<tr>
<th>Study/Year</th>
<th>No. of Cases</th>
<th>True Infection % (n/N)</th>
<th>Deaths</th>
<th>Epidemiologic Link</th>
<th>Etiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bou et al[23]/2006</td>
<td>13</td>
<td>100 (13/13)</td>
<td>NA</td>
<td>Random arbitrary polymorphic DNA-PCR</td>
<td>User noncompliance</td>
</tr>
<tr>
<td>Corne et al[24]/2005</td>
<td>18</td>
<td>22.2 (4/18)</td>
<td>0</td>
<td>Antibiotic susceptibility, PFGE</td>
<td>Damaged internal channel</td>
</tr>
<tr>
<td>Kirschke et al[25]/2003</td>
<td>20</td>
<td>5 (1/20)</td>
<td>NA</td>
<td>PFGE</td>
<td>Manufacturing defect</td>
</tr>
<tr>
<td>Srinivasan et al[26]/2003</td>
<td>97</td>
<td>33 (32/97)</td>
<td>3</td>
<td>PFGE</td>
<td>Manufacturing defect</td>
</tr>
<tr>
<td>Silva et al[27]/2003</td>
<td>41</td>
<td>0 (0/41)</td>
<td>0</td>
<td>Ribotyping</td>
<td>Lack of strict disinfection methods</td>
</tr>
<tr>
<td>Sorin et al[28]/2001</td>
<td>18</td>
<td>17 (3/18)</td>
<td>1</td>
<td>PFGE</td>
<td>User noncompliance</td>
</tr>
<tr>
<td>Schelzen and French[29]/2000</td>
<td>11</td>
<td>NA</td>
<td>2</td>
<td>Serotype, phage type, REP-PCR</td>
<td>Contaminated washer-disinfector</td>
</tr>
<tr>
<td>Blanc et al[30]/1997</td>
<td>23</td>
<td>NA</td>
<td>NA</td>
<td>Ribotyping</td>
<td>Contamination by washing machine</td>
</tr>
<tr>
<td>Kolmos et al[31]/1994</td>
<td>8</td>
<td>0 (0/8)</td>
<td>0</td>
<td>Serotype</td>
<td>User noncompliance</td>
</tr>
<tr>
<td>Sammartino et al[32]/1982</td>
<td>11</td>
<td>9 (1/11)</td>
<td>0</td>
<td>Serotype</td>
<td>Lack of disinfection guidelines</td>
</tr>
<tr>
<td>Hussain[33]/1978</td>
<td>7</td>
<td>14 (1/7)</td>
<td>NA</td>
<td>Antibiotic susceptibility pattern</td>
<td>User noncompliance</td>
</tr>
</tbody>
</table>

n = number of patients with true *P. aeruginosa* infection; N = total number of patients with isolates of *P. aeruginosa*; PCR = polymerase chain reaction; PFGE = pulsed-field gel electrophoresis; REP-PCR = repetitive DNA sequence-based PCR. See Table 1 legend for expansion of the other abbreviations.
Bronchoscope contamination has been associated with defective design, damage of the bronchoscopes, and improper use of the disinfection process. Precipitating factors included: a loose biopsy-port cap in one bronchoscopes model leading to a cluster of *P aeruginosa* pneumonia with three possible deaths, a damaged internal channel caused by defective biopsy forceps, contamination by a washing machine, and inadequate disinfection of bronchoscopes. Two pseudo-outbreaks were reported with isolation of *P aeruginosa* in eight and 41 patients undergoing bronchoscopy, respectively; none of the pneumonias was documented to be associated with the outbreak strains.

**Community-Acquired Pneumonia**

Observational studies show that *P aeruginosa* is a rare cause of CAP. *P aeruginosa* was the etiologic microbe in 0.9% to 1.9% of patients with CAP requiring hospitalization. In a meta-analysis of 33,148 patients with CAP in 127 study cohorts, only 18 cases of *P aeruginosa* infection were documented, with a crude mortality rate of 61.1% (11/18). In a 2000 review of published cases of *P aeruginosa* CAP in previously healthy adults using strict criteria in which *P aeruginosa* was documented by isolation of organism in blood, lung tissue, or pleural fluid, only 12 cases had been reported in the world literature.

On the other hand, in investigations of CAP performed in ICUs, *P aeruginosa* is listed as a pneumonia pathogen, although an uncommon one. In patients with severe CAP, defined as CAP necessitating admission to ICUs or having shock, *P aeruginosa* was the cause in 1.8% to 8.3% with a case-fatality rate of 50% to 100%. In one ICU study, *P aeruginosa* was the third most identifiable cause of CAP. (The first and second most common causes are usually *Streptococcus pneumoniae* and *Legionella pneumophila.*) All of these ICU studies had methodological weaknesses with respect to confirmation of *P aeruginosa* as the causative pathogen. Only 44.4% to 78.6% of the patients had a definitive microbiologic diagnosis.

None of the previous studies explicitly described the duration between previous and current hospitalization and whether patients met the criteria of health-care-associated pneumonia. Health-care associated pneumonia in one study was defined as hospitalization within 30 days or 1 year in another study. In these two studies, the cause was *P aeruginosa* in 17.1% and 4.8% of cases with CAP, respectively, and 25.3% and 25.5% of health-care-associated pneumonia, respectively. In contrast, in a prospective study of 5,130 patients, the German Community-Acquired Pneumonia Competence Network study group identified 22 patients with *P aeruginosa* as the causative pathogen using rigorous criteria: isolation from blood (one patient) and isolation confirmed by Gram stain (21 patients). This constituted an incidence of only 0.4% (22/5,130). Mortality was 18%. In a Spanish prospective study of 780 patients with CAP, *P aeruginosa* was rare.

Risk factors for CAP caused by *P aeruginosa* have been well elucidated. Lung disease, especially COPD, is a consistent risk factor. Other risk factors, including previous hospitalization, intubation, and enteral tube feeding are all consistent with colonization being an important antecedent event; these cases may actually be more accurately classified as health-care-associated pneumonia. *P aeruginosa* is listed as a pathogen of CAP in patients with COPD and/or smoking, HIV infection, and structural lung disease (eg, bronchiectasis).

**P aeruginosa Pneumonia in Patients With HIV**

Before the era of highly active antiretroviral therapy (HAART), HIV-positive adults had a significantly higher rate of bacterial pneumonia than HIV-negative adults (5.5 vs 0.9/100 person-years, *P* < .01), and the rate increased with decreasing CD4 lymphocyte counts. In the pre-HAART era, *Streptococcus pneumoniae* remained the most common cause (25%-46.7%), whereas *P aeruginosa* was the cause in 8% to 25%. As for hospital-acquired pneumonia, *P aeruginosa* was the most common bacterial pathogen (21.4%-38.7%). The mortality related to *P aeruginosa* pneumonia ranged from 42% to 55%, which was much higher than that of pneumonias caused by other organisms. CAP by *P aeruginosa* occurred in 16 patients with HIV with a mean CD4 count of only 27 cells/μL; 69% of the patients had cavitary infiltrates on chest radiograph. Traditional risk factors for *P aeruginosa*, such as neutropenia, recent hospitalization, or previous antimicrobial treatment, were absent. Prophylaxis with trimethoprim-sulfamethoxazole for *Pneumocystis* pneumonia was associated with significant protection from *Toxoplasmosis, Salmonella, Haemophilus*, and *Staphylococcus aureus*, but not *S pneumoniae* or nonpneumococcal *Streptococcus* or *P aeruginosa*.

HAART has notably decreased morbidity and mortality in patients with advanced HIV infection. However, a declining incidence of bacterial pneumonia has not been consistently shown, and bacterial pneumonia remains the most common cause of hospitalization. *S pneumoniae* is still the most common cause (30%-35.7%) of community-acquired bacterial pneumonia in the HAART era, although *P aeruginosa* contributes to 5% to 6.7% of the cases. The most common bacterial pathogen for nosocomial pneumonia in patients with HIV remains *P aeruginosa*, with a mortality of 23%. Patients with *P aeruginosa* pneumonia have CD4 counts comparable to those in the pre-HAART era. The median...
Diagnosis

The diagnosis of pneumonia caused by *P. aeruginosa* can be challenging given the relative ease of colonization in the upper and lower respiratory tract. Except for the syndrome of pneumonia in neutropenic or highly immunosuppressed hosts, blood cultures are rarely positive in patients with *Pseudomonas* pneumonia in the hospital-acquired setting. In the intubated patient, *P. aeruginosa* may be isolated consistently from endotracheal cultures for prolonged periods, often without signs of systemic infection. Purulent sputum or endotracheal aspirates may be unreliable given the presence of tracheobronchitis, although tracheobronchitis may be a precursor to subsequent pneumonia. Gram stains have not proven useful. Many pragmatic clinicians believe that an abrupt increase in quantity and purulence of respiratory secretions should lower the threshold for antibiotic treatment. For patients with VAP, the presence of intracellular organisms in centrifuged BAL fluid has been shown to be a specific marker for infection. Sensitivity ranged from 37% to 100%.

Colonization vs Infection

*P. aeruginosa* has been isolated from sputum in 4% to 15% of adults with COPD without pneumonia. Prior antibiotic use is a risk factor for *P. aeruginosa* colonization. Broad-spectrum antibiotics can lead to increased colonization of *P. aeruginosa* in ICUs; *P. aeruginosa* was the dominant species colonizing endotracheal aspirates. *P. aeruginosa* enhances mucus secretion, disrupts ciliary activity, and causes airway epithelial injury, thereby impairing pulmonary clearance. *P. aeruginosa* isolated from the respiratory tract tend to be antibiotic resistant, produce fewer virulence factors, and produce more biofilm as compared with *P. aeruginosa* isolated from the blood of patients in the ICU. *P. aeruginosa* can be isolated from the lung 8 days after onset of VAP despite active antibiotic therapy. Recurrent episodes of *P. aeruginosa* VAP are usually due to persistence of *P. aeruginosa* from prior infection as determined by molecular subtyping. Because bacteremia is very rare in hospital-acquired *P. aeruginosa* pneumonia, definitive confirmation of the etiologic role of *P. aeruginosa* is difficult. Thus, isolation of *P. aeruginosa* from respiratory secretions in which clinical manifestations of pneumonia exist with a new pulmonary infiltrate is often considered to be circumstantial evidence that *P. aeruginosa* is the cause and becomes the basis for initiation of antipseudomonal antibiotic therapy.

In a prospective, double-blind comparative antibiotic trial in patients with health-care-associated pneumonia, two patients with pneumonia and *P. aeruginosa* isolated from sputum cultures received empirical ertapenem, which has inadequate in vitro activity against *P. aeruginosa*. Both patients responded to therapy. In our experience, we encountered two patients in whom the Clinical Pulmonary Infection Score (CPIS) was < 7 and therefore did not warrant combination therapy of prolonged duration. One of two patients had COPD. On day 3, respiratory cultures yielded *P. aeruginosa* as the predominant microbe; however, the CPIS score remained low. Empiric therapy with a quinolone had been initiated as part of the CPIS protocol. In both patients, the *P. aeruginosa* ultimately isolated was resistant in vitro to the quinolone. Because the CPIS was low, the quinolone was discontinued on day 3 as per protocol. The pulmonary infiltrate improved gradually in both patients without further antipseudomonal therapy. Both patients remained stable, although *P. aeruginosa* was isolated from the respiratory tract for many weeks thereafter. These anecdotes are circumstantial evidence that *P. aeruginosa* is a colonizer, and that the pulmonary infiltrates did not necessarily represent infection. Additionally, it calls into question the high frequency of *P. aeruginosa* pneumonias reported from the ICU setting, because colonization is clearly a confounding factor.

In a surveillance study of ICUs in a tertiary care center, daily surveillance culture of endotracheal aspirates were performed on intubated patients. Forty-five patients showed high quantitative counts of *P. aeruginosa*. Seventeen (37.8%) patients did not fulfill clinical criteria for VAP; new or progressive infiltrates on chest radiograph were not visualized on the day of the cultures. Yet, their risk for death was high (in fact, higher than those with *P. aeruginosa* that fulfilled the criteria for VAP). Moreover, it has been shown that in stable patients receiving mechanical ventilation for prolonged periods (months), alveolar colonization with high bacterial burdens could be found in patients without pneumonia. Limiting antibiotics in patients in the ICU with pulmonary infiltrates with CPIS ≤ 6 did not lead to higher mortality; in fact, mortality decreased. We suggest that the *P. aeruginosa* isolated from many patients in the ICU with pulmonary infiltrates may merely be a marker for prolonged ICU stay and increased mortality, but not a true pulmonary pathogen that requires intensive antibiotic therapy.

Diagnostic Approaches

Invasive procedures with quantitative cultures have been proposed, but failure to control for concomitant antibiotics, nonstandardization of techniques, and inconsistent gold standards have confounded the many attempts to establish a clear-cut diagnostic approach of choice. Three approaches that have been assessed in randomized trials appear to be practicable in patients with suspected pneumonia.

1. In an impressive controlled trial of 413 patients in 31 French ICUs, an invasive approach used for diagnosis of VAP minimized broad-spectrum antibiotic use and improved mortality. Using protected brush bronchoscopy and
Endotracheal aspirates with quantitative cultures is an approach that can be readily applied. This approach was compared with BAL with quantitative cultures in a multicenter randomized trial of 740 patients in 28 ICUs in North America. The outcomes and overall use of antibiotics was similar for both groups. An important caveat is that patients with *P. aeruginosa* were excluded.

3. The CPIS was used to decide if empirical antibiotic therapy could be limited to one antibiotic given for 3 days in patients with pulmonary infiltrates. This approach was not used to determine with certainty whether pneumonia was actually present; nevertheless, a low score implied that the risk for infection was low and the patient was clinically stable. This is a pragmatic approach for management and a safe alternative to the current strategy of prolonged broad-spectrum empirical antibiotic therapy. Given that colonization is often difficult to distinguish from pneumonia, this approach can maximize patient protection from an infection without subjecting the patient to the risks of superinfection by a resistant *P. aeruginosa* and the adverse effects of antibiotics prescribed. Reevaluation after 3 days with culture results could allow the antibiotic to be safely discontinued.

### Radiologic Findings

The “classic” radiologic description of *P. aeruginosa* pneumonia was formulated by Tillotson and Lerner in 1968 when they described 10 patients with nonbacteremic *P. aeruginosa* pneumonia. *Pseudomonas* pneumonia was characterized as a diffuse bronchopneumonia with nodularity and “small areas of radiolucency (‘microabcesses’).” Of note, subsequent pathologic correlates suggested that the microabcesses were actually areas of normal or emphysematous lung surrounded by an infected infiltrated lung, the “air-alveolograms.”

Subsequent studies have failed to confirm the conclusions of Tillotson and Lerner. Although the original report described features of nodularity in 100% (10/10) of the study cases, two later studies showed nodularity in only 22% (5/23) and 50% (14/28). A minority of cases (10%-35%) showed cavity or abscess formation, with one outlying study showing 84% of cases with this feature. The most consistent finding was a bilateral distribution of infiltrates, present in 48% to 91% of cases. One study suggested that rapid progression from pulmonary vascular congestion to a pulmonary edema pattern and finally to a necrotizing bronchopneumonia was commonplace. We conclude that a specific pattern of radiologic features for *P. aeruginosa* pneumonia does not exist and chest radiology cannot be used to make a specific diagnosis of pneumonia due to *P. aeruginosa*.

### Source of *Pseudomonas aeruginosa*

#### Colonization

Respiratory tract colonization by *P. aeruginosa* is the precursor for development of hospital-acquired pneumonia. In ICUs, respiratory tract colonization with *P. aeruginosa* has been significantly associated with duration of ICU stay, duration of mechanical ventilation, and prior antibiotic use. *P. aeruginosa* colonization of hospitalized patients can result from admission of patients already colonized within their oropharynx or their GI tract. Fresh fruits and vegetables have been documented in a few outbreaks; however, confirmatory studies supporting this widespread supposition are lacking.

### Tap Water as a Source

Although cross-transmission of *P. aeruginosa* has been documented in a few outbreaks, a more likely source is the environment. Interestingly, *P. aeruginosa* from the hospital environment (as opposed to cross-transmission from other patients) possessed a higher level of resistance to antipseudomonal antibiotics. These environmental isolates were also more likely to colonize and infect other patients as compared with pre-existing isolates colonizing other patients. Tap water containing *P. aeruginosa* used for surgical procedures or irrigation of medical instruments can lead to hospital-acquired *P. aeruginosa* infections, including bacteremia and abdominal infections. Bronchoscopy-associated respiratory infection was described earlier in this review; tap water was likely the source in some of these instances.

In some hospitals, tap water may be an important source of *P. aeruginosa*. Eighteen studies with populations of three to 7,269 patients and duration of 3 months to 3 years investigated the sources of *P. aeruginosa* outbreaks (n = 6) or patients with *P. aeruginosa* infection/colonization (n = 12) in ICUs. In all, 14 of the studies concluded tap water, faucets, or sinks could be the source; eight studies reported transmission between patients or health-care workers; and two studies found that the endogenous flora of patients themselves was the source. Transmission is facilitated by the fact that *P. aeruginosa* can survive...
for months on inanimate surfaces and for 3 h on hands of health-care givers.[130]

In the 14 studies, *P aeruginosa* could be isolated from 9.1% to 97% of the tap water/faucet/sink samples. Using molecular subtyping, the proportion of the *P aeruginosa* isolated from patients, which was identical to those isolated from the tap water/faucets/sinks, ranged from 19.2% to 100%. *P aeruginosa* colonization can originate from hospital tap water, but patient strains might also contaminate hospital water supplies. Two studies demonstrated that 40% to 46.7% of the patients with *P aeruginosa* were possibly infected by tap water, whereas 11% to 52.4% of faucet samples were possibly contaminated by patients. [118] . [128]

Cross-transmission was found in 29.5% to 52.6% of the patients based on isolation of *P aeruginosa* of identical molecular subtyping found in other patients. *P aeruginosa* could be isolated from 3% to 6% of the hands of health-care workers, and 10% to 20% of these isolates were genotypically related to patient isolates. [115] . [120] . [121] . [128]

Seven studies described infection control solutions. The source originated from a health-care worker in one study, and the outbreak ceased after reassignment of the health-care worker to nonclinical activities along with other infection control measures. [121] Tap water, faucets, or sinks were considered to be the source in the six remaining studies; three of them changed or regularly replaced faucet aerators, sinks, shower heads, and hoses; two disinfected the water with increased water temperature, copper and silver ionization, or chlorination [123] . [127] ; and three used water filters [129] . [127] . [129] ; two reinforced infection-control precautions. [123] . [127] In an outbreak involving 36 patients infected with a single strain of a multidrug-resistant *P aeruginosa*, the source was traced to a sink used for handwashing. The sink was adjacent to a counter used for medical procedures and drug preparation and close to patient beds. [131] The outbreak was aborted when splash barriers were installed.

The most impressive interventional measures have been the installation of water filters that not only decreased the growth of *P aeruginosa* in tap water but also significantly decreased *P aeruginosa* colonization by 85% and subsequent invasive infections. [129] . [132] Disinfection of faucets and replacement of shower heads and hoses proved ineffective [112] . [127] ; similar findings have been documented for health-care-associated Legionnaires disease. High water temperature and copper and silver ionization decreased the annual incidence of patients colonized or infected with *P aeruginosa*, although biofilm colonization of faucets with *P aeruginosa* persisted. [123] Anaissie et al [133] recommended the use of sterile water for drinking, brushing teeth, and flushing of nasogastric tubes. Interestingly, tap water has been shown to be a common source of *P aeruginosa* in malignant (necrotizing) external otitis, a disease inextricably linked to *P aeruginosa*. [134]

**Conclusions**

Several distinct clinical syndromes of pneumonia due to *P aeruginosa* exist. The most common presentation of pneumonia involving *P aeruginosa* is hospital-acquired ICU pneumonia; mortality and monetary costs remain unacceptably high. Although CAP is uncommon and usually occurs in patients with chronic lung disease, the high attributable mortality is similarly concerning. HIV infection with bacteremic dissemination is a relatively new presentation. Bacteremic pneumonia in patients who are immunosuppressed, especially patients who are neutropenic, has decreased in frequency, probably due to advances in cancer chemotherapy.

Diagnosis of *P aeruginosa* pneumonia is complicated by the fact that isolation from respiratory tract cultures may represent colonization instead of infection, especially in patients with COPD or those with prolonged hospital stay. Antipseudomonal antibiotic therapy based on respiratory tract cultures may therefore lead to overtreatment. Invasive procedures with quantitative cultures have proven to be effective in selecting patients who would benefit from antimicrobial therapy. An alternative, less-invasive approach using the CPIS as a guide for empirical therapy appears effective in minimizing overtreatment with antibiotics. Because tap water may be a source for *P aeruginosa* in some ICUs, preventive measures directed at the water may reduce colonization and subsequent infection rates.

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