Management and Outcome Patterns for Adult *Pneumocystis carinii* Pneumonia, 1985 to 1995* 
Comparison of HIV-Associated Cases to Other Immunocompromised States

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**Study objectives:** Encompassing periods preceding and following major advances in the diagnosis and management of HIV-related *Pneumocystis carinii* pneumonia (PCP), the purpose of this study was to determine whether management and outcome patterns of non-HIV PCP parallel the management and outcomes of AIDS-related PCP.

**Design:** Retrospective review of medical records.

**Setting:** A 375-bed tertiary-care urban teaching hospital and referral center.

**Patients:** All adult patients with morphologically confirmed PCP from 1985 to 1995.

**Measurements and results:** From 1985 to 1995, 638 confirmed cases of PCP were identified, including 605 cases in 442 HIV-positive persons (HIV+ PCP), and 33 cases in 33 non-HIV patients (non-HIV PCP). For HIV+ PCP cases, a peak of 104 cases occurred in 1987, with a gradual decline to 23 in 1995. The proportion of cases requiring hospitalization declined from a peak of 91.6% in 1987 to a low of 51.6% in 1992. ICU admission was required for 6.3% to 8.2%, and mechanical ventilation for 4.7% to 5.7%. Overall mortality improved from 11.7% to 6.6%, although mortality for intubated patients remained at 50% to 60%. For the non-HIV PCP cases, 97% occurred from 1989 to 1995 with similar annual frequency, 97% required hospitalization, 69% required ICU admission, and 66% required intubation. Overall mortality was 39%, and mortality for intubated patients was 59%.

**Conclusions:** Despite major advances in diagnosis and management, PCP remains a significant problem in non-HIV-infected patients, and respiratory failure remains associated with a high mortality rate for patients with both HIV + PCP and non-HIV PCP.

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**Key words:** AIDS; HIV; immunosuppression; mechanical ventilation; mortality; *Pneumocystis carinii* pneumonia

**Abbreviations:** BIDMC = Beth Israel Deaconess Medical Center; HAART = highly active antiretroviral therapy; HIV + PCP = HIV-associated PCP; Non-HIV PCP = PCP associated with other immunodeficiency states; PCP = *Pneumocystis carinii* pneumonia

The management of *Pneumocystis carinii* pneumonia (PCP) in persons infected with HIV type-1 has evolved substantially since the beginning of the AIDS epidemic. Early in the epidemic, PCP occurred in up to 75% of HIV-infected individuals. Since 1989, several important advances greatly influenced the management of AIDS-related PCP, including the use of CD4+ T lymphocyte counts to identify persons at high clinical risk for PCP; the prescription of prophylactic agents to persons at high clinical risk; the availability of more sensitive immunofluorescence methods of *P carinii* detection; the availability of newer antimicrobial agents; the introduction of adjunctive corticosteroids for treating moderate-to-severe PCP; the use of aggressive

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supportive interventions and monitoring\textsuperscript{9–12}; and the use of effective combination antiretroviral treatment.\textsuperscript{13} Collectively, these advances likely in part contributed to the reduced incidence and improved mortality for HIV-associated PCP (HIV + PCP),\textsuperscript{14} improvements which were recognized prior to the introduction of highly active antiretroviral therapy (HAART).\textsuperscript{15,16}

In contrast to AIDS-related cases, cases of PCP in patients with other predisposing immunodeficiency states\textsuperscript{17–23} (uncommon prior to the AIDS epidemic) may be increasing\textsuperscript{24,25} and the associated mortality may be \( > 50\% \).\textsuperscript{19–21,25} Furthermore, management of PCP associated with other immunodeficiency states (non-HIV PCP) is less standardized. For example, PCP chemoprophylaxis is routinely prescribed for recent organ transplant recipients (traditionally recognized at high clinical risk for PCP), while the role for chemoprophylaxis for individuals receiving long-term corticosteroid therapy (traditionally considered at some, although undefined, risk) has not been established.\textsuperscript{23} Furthermore, the duration of prophylaxis required for solid organ transplant recipients\textsuperscript{26} and the role for acute heightened-dose adjunctive corticosteroids for the treatment of non-HIV PCP remain undefined.\textsuperscript{22}

Recognizing differences in clinical and laboratory characteristics comparing HIV + PCP to non-HIV PCP,\textsuperscript{19,27} a prior report suggested similar high mortalities of 57\% and 50\%, respectively.\textsuperscript{19} However, as with most recent large series,\textsuperscript{19,21,24,28} these reports included data prior to the major advances in the management of AIDS-related PCP. Of the reports that include cases since 1990,\textsuperscript{23,25} no comparison to HIV + PCP is included. Although several investigators have suggested that advances in the management of HIV + PCP may be applied to non-HIV PCP,\textsuperscript{20,29,30} specific studies related to non-HIV PCP are limited; whether the significant changes in management and outcomes of non-HIV PCP paralleled the changes associated with advances in HIV + PCP management remains to be determined. Reviewing an 11-year period during the AIDS epidemic, and including periods before and after the introduction of major advances in the diagnosis and treatment of AIDS-related PCP, the purpose of this study was to examine the management patterns and clinical outcomes of PCP at a tertiary-care urban hospital comparing cases in HIV-infected persons to cases in other immunocompromised persons without HIV infection.

**Materials and Methods**

**Setting**

The Beth Israel Deaconess Medical Center (BIDMC), West Campus is a 375-bed tertiary-care urban teaching hospital and referral center. The hospital provides extensive inpatient and outpatient care for a population of \( > 1,400 \) HIV-positive patients. In addition, the BIDMC provides care for a diverse population of immunocompromised medical and surgical patients on various services, including active hepatic and renal transplant services, hematology and oncology services, and general medical service. The BIDMC includes active ICUs for medical, cardiac, cardiothoracic, surgical, and vascular patients.

**Identification of PCP Cases**

Confirmed cases of PCP were identified by a retrospective review of detailed microbiological and pathologic records that identified PCP in biological specimens for the period from 1985 to 1995. These years represented a period for which complete medical information was available, and also included the period preceding and following major advances in the care of AIDS-related PCP. Biological specimens from inpatient and outpatient services included respiratory tract specimens (induced sputa, BAL, transbronchial biopsies), pleural fluid analysis, and surgical tissue biopsy. All requests for induced sputum and BAL specimens were administered through the Division of Pulmonary Medicine and were detailed in comprehensive log books.

Only cases demonstrating *P carinii* organisms by immunofluorescence, modified Giemsa, or methenamine silver staining in specimens of induced sputum, BAL, transbronchial or open lung biopsy, or other biological specimens were included in the study. Presumptive cases of PCP were excluded. The demonstration of typical *P carinii* organisms in respiratory tract specimens within 30 days of a documented episode of PCP was considered as a single event.

**Patient Demographics and Clinical Outcomes**

Outpatient and inpatient medical records of all identified confirmed cases in patients \( > 18 \) years of age were reviewed, and information was recorded on standardized forms, including age, gender, underlying medical conditions, HIV status and risk factors, peripheral CD4 T-lymphocyte count, use of immunosuppressive agents prior to PCP diagnosis, and use of chemoprophylaxis against *P carinii*. Ethnicity data were not available.

The measured outcomes included requirement for hospitalization, ICU admission, intubation, and associated mortalities. To accurately identify all patients requiring intubation and mechanical ventilation, medical records data were cross-referenced with the log books of the ICU and respiratory therapists. Respiratory failure was defined as requiring endotracheal intubation and mechanical ventilation support. All persons with HIV + PCP were documented HIV seropositive. All non-HIV cases were documented HIV seronegative.

**Statistical Analysis**

For the statistical analysis, continuous data were compared with use of the Student’s *t* test\textsuperscript{31} and confirmed by the Mann-Whitney test. Statistical analysis of noncontinuous dichotomous data were compared by the \( \chi ^2 \) test (with Yates correction) or the Fisher’s Exact Test as appropriate.\textsuperscript{32} All statistical analysis were performed on an IBM PS/2 computer (IBM; Armonk, NY) utilizing INSTAT2 statistical program (Graphpad Software; San Diego, CA). All \( p \) values were two sided, and statistical significance was accepted for \( p < 0.05 \).
Results

Characteristics of Confirmed Cases of PCP

A total of 670 confirmed cases of PCP in adult patients were identified for the period from 1985 to 1995. These cases included 637 episodes of PCP in 474 HIV-seropositive individuals (HIV + PCP), and a total of 33 cases in 33 individuals with other immunocompromised states (non-HIV PCP). Medical records for 605 HIV + PCP cases and for all 33 non-HIV PCP cases were available for review. The clinical characteristics of the identified patients are presented in Table 1. The mean age for non-HIV PCP patients was higher, compared to HIV + PCP patients (37.5 ± 6.8 years vs 57.8 ± 9.8 years; p = 0.032). Although male patients represented the majority of cases for both groups, female patients accounted for a greater proportion of non-HIV PCP cases (33% vs 5.2%; p = 0.0001). All cases were diagnosed antemortem.

Distribution of Confirmed Cases of PCP in Immunocompromised Patients

Figure 1 presents the annual number of confirmed cases of PCP for the study period. For HIV + PCP (Fig 1, top, A) the number of confirmed cases of PCP peaked in 1987 with 104 cases, and gradually declined to 23 cases in 1995. For non-HIV PCP (Fig 1, bottom, B), only one patient was identified prior to 1989, whereas 32 of 33 cases (97%) were identified since 1989 with a relatively constant annual frequency.

Hospitalization vs Outpatient Management of PCP

The management and outcomes for confirmed cases of PCP are summarized in Table 2. For HIV + PCP, the proportion of episodes requiring hospitalization gradually decreased over the period from 1985 to 1993. In 1985, 85.7% of episodes were hospitalized, whereas by 1993, only 50.0% of all confirmed cases were hospitalized. The proportion requiring hospitalization increased in the last 2 years of the study to 80 to 93%, although the total number of confirmed cases continued to decline. In contrast to the HIV + PCP group, only one of the non-HIV PCP patients received outpatient therapy, whereas 97% of patients required hospitalization.

ICU Admission and Requirement for Mechanical Ventilation

For hospitalized patients, 9.8% of all episodes of HIV + PCP required ICU admission, and 7.3% of all episodes resulted in intubation and mechanical ventilation. Of the 43 individuals requiring ICU.
admission, 74.4% were for respiratory failure requiring mechanical ventilation. In comparison, for the non-HIV PCP patients, 68.8% required ICU admission, and overall 65.6% required intubation and mechanical ventilation. Of the 22 patients requiring ICU admission, 95.5% were for respiratory failure.

**Mortality for PCP**

The overall mortality for the HIV + PCP group was 9.6%, and hospital mortality was 13.2%. For patients with acute respiratory failure requiring intubation, the mortality was 56.2%. In comparison, the overall mortality for the non-HIV PCP patients was 39.4% (p < 0.0001, compared to HIV + PCP), in-hospital mortality was 40.6% (p < 0.0001), and the mortality for non-HIV PCP patients who required intubation and mechanical ventilation was 59.1% (p = 1.0).

**Trends in Outcomes in PCP From 1985 to 1995**

The trends for ICU admission, intubation, and mortality rates are presented in Figure 2. For HIV + PCP cases, the proportion of patients requiring hospitalization declined from a peak of 91.6% in 1987 to a low of 51.6% in 1992. For the hospitalized patients, the need for ICU admission and mechanical ventilation peaked in 1991, corresponding to the introduction of adjunctive corticosteroids (Fig 2, top, A). Overall mortality ranged from 3.4 to 14.8%, and mortality for intubated patients was 0 to 80%. In comparison, for non-HIV PCP, all patients since 1989 required hospitalization, and the rates of ICU admission, intubation, and mortality remained consistently high (Fig 2, bottom, B).

Recognizing the importance of adjunctive corticosteroids in the management of HIV + PCP, data were reviewed comparing the interval from 1985 to 1989, to 1990 to 1995 (corresponding to the periods prior to and following the routine use of adjunctive corticosteroids for moderate-to-severe HIV + PCP; Table 3). The proportion of HIV + PCP patients requiring hospitalization decreased from 79.3 to 62.3% (p < 0.001), although no significant change in ICU admission rates was observed, 6.3% vs 8.2% respectively (p = 0.09). The overall mortality decreased from 11.8 to 6.6% (p = 0.036), although the mortality for intubated patients remained high and unchanged at 60% and 50%, respectively (p = 0.718). For the corresponding time intervals for non-HIV PCP (recognizing that the approach to the management of non-HIV PCP is less standardized), rates remained high with no significant differences in hospitalization rates.

### Table 2—Clinical Management and Outcomes in Patients With Confirmed PCP at the BIDMC, 1985 to 1995*

<table>
<thead>
<tr>
<th>Variables</th>
<th>HIV-Positive Patients</th>
<th>Non-HIV-Infected Patients</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total episodes, No.</td>
<td>605</td>
<td>33</td>
<td></td>
</tr>
<tr>
<td>Outpatient management, No. (%)</td>
<td>167 (27.6)</td>
<td>1 (3.0)</td>
<td>0.0008</td>
</tr>
<tr>
<td>Hospitalized, No. (%)</td>
<td>438 (72.4)†</td>
<td>32 (97.0)†</td>
<td></td>
</tr>
<tr>
<td>ICU admission</td>
<td>43 (9.8)†</td>
<td>22 (68.8)†</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Intubation</td>
<td>32 (7.3)†</td>
<td>21 (65.6)†</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Discharged from ICU</td>
<td>25 (58.1)‡</td>
<td>9 (40.9)‡</td>
<td>NS</td>
</tr>
<tr>
<td>Mortality, No. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All episodes</td>
<td>58 (9.6)</td>
<td>13 (39.4)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Hospitalized patients</td>
<td>58 (13.2)</td>
<td>13 (40.6)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Intubated patients</td>
<td>18 (56.2)</td>
<td>13 (59.1)</td>
<td>NS</td>
</tr>
</tbody>
</table>

* NS = not significant.
† Percentage of hospitalized patients.
‡ Percentage of ICU admissions.

![Figure 2](http://journal.publications.chestnet.org/pdfaccess.ashx?url=data/journals/chest/21952/)
Outcomes comparing HIV-infected patients to individuals with other underlying immunodeficiency states. Over the period from 1985 to 1995, the number of confirmed HIV + PCP cases declined at our medical center, and the rate of hospitalization for the management of PCP declined. The rates of ICU admission and respiratory failure requiring mechanical ventilation peaked coincident with the introduction of adjunctive corticosteroids, but overall were 7.0% and 5.2%, respectively. The overall mortality ranged from 3.4 to 14.8%, although mortality in patients with acute respiratory failure requiring mechanical ventilation remained at 50 to 60%. A decline in hospitalization rates and overall mortality was especially evident, comparing 1985 to 1989 (corresponding to the period prior to the routine use of corticosteroids for moderate-to-severe PCP) with 1990 to 1995 (the period corresponding to the routine use of adjunctive corticosteroids).

In contrast, the number of confirmed cases of PCP identified in patients with other immunocompromised states increased over the period from 1985 to 1995, particularly during the latter half of this period. Only one case was identified prior to 1989, whereas 97% of confirmed cases were identified since 1989 at this institution. Importantly, the rates of hospitalization, ICU admission, intubation with mechanical ventilation, and mortality for the non-HIV PCP group remained high, where 97% of the confirmed cases required hospitalization, 68.8% required ICU admission, and 65.6% required intubation and mechanical ventilation. The overall mortality for these patients was 39.4%, and the mortality for those experiencing acute respiratory failure and requiring intubation was 59.1%. For the period from 1990 to 1995, these outcomes were worse than for HIV + PCP in this study, and these outcomes were similar to published reports from other institutions made prior to the advances for HIV + PCP.21,25,28

The explanation for the progressive decline in the number of cases of HIV + PCP was not specifically addressed in this retrospective review. The decline was not associated with a decline in the population of HIV-positive patients followed at our institution.

### Discussion

This study demonstrates that significant differences have evolved in PCP management and clinical outcomes comparing HIV-infected patients to individuals with other underlying immunodeficiency states. Over the period from 1985 to 1995, the number of confirmed HIV + PCP cases declined at our medical center, and the rate of hospitalization for the management of PCP declined. The rates of ICU admission and respiratory failure requiring mechanical ventilation peaked coincident with the introduction of adjunctive corticosteroids, but overall were 7.0% and 5.2%, respectively. The overall mortality ranged from 3.4 to 14.8%, although mortality in patients with acute respiratory failure requiring mechanical ventilation remained at 50 to 60%. A decline in hospitalization rates and overall mortality was especially evident, comparing 1985 to 1989 (corresponding to the period prior to the routine use of corticosteroids for moderate-to-severe PCP) with 1990 to 1995 (the period corresponding to the routine use of adjunctive corticosteroids).

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### Table 3—Outcomes in Confirmed Episodes of PCP Comparing the Periods Prior to and Following the Routine Use of Adjunctive Corticosteroids for AIDS-Associated PCP

<table>
<thead>
<tr>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV+ PCP</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total episodes, No.</td>
<td>348</td>
<td>257</td>
<td></td>
</tr>
<tr>
<td>Prophylaxis, %</td>
<td>53.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospitalization, No. (%)</td>
<td>276 (79.3)</td>
<td>160 (62.3)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>ICU admission</td>
<td>22 (6.3)</td>
<td>21 (8.2)</td>
<td></td>
</tr>
<tr>
<td>Intubation</td>
<td>20 (5.7)</td>
<td>12 (4.7)</td>
<td></td>
</tr>
<tr>
<td>Mortality, No. (%)</td>
<td>12 (60.0)</td>
<td>6 (50.0)</td>
<td></td>
</tr>
<tr>
<td>All episodes</td>
<td>41 (11.8)</td>
<td>17 (6.6)</td>
<td>0.036</td>
</tr>
<tr>
<td>Non-HIV PCP</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total episodes, No.</td>
<td>3</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>Prophylaxis, %</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Hospitalization</td>
<td>2 (66.7)</td>
<td>30 (100)</td>
<td>NS</td>
</tr>
<tr>
<td>ICU admission</td>
<td>1 (33.3)</td>
<td>21 (70.0)</td>
<td></td>
</tr>
<tr>
<td>Intubation</td>
<td>0 (0)</td>
<td>21 (70.0)</td>
<td>0.04</td>
</tr>
<tr>
<td>Mortality, No. (%)</td>
<td>0 (0)</td>
<td>12 (57.1)</td>
<td>NS</td>
</tr>
<tr>
<td>All episodes</td>
<td>0 (0)</td>
<td>13 (43.3)</td>
<td></td>
</tr>
<tr>
<td>Non-HIV-infected patients</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total episodes, No.</td>
<td>3</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>Prophylaxis, %</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Hospitalization</td>
<td>2 (66.7)</td>
<td>30 (100)</td>
<td>NS</td>
</tr>
<tr>
<td>ICU admission</td>
<td>1 (33.3)</td>
<td>21 (70.0)</td>
<td></td>
</tr>
<tr>
<td>Intubation</td>
<td>0 (0)</td>
<td>21 (70.0)</td>
<td>0.04</td>
</tr>
<tr>
<td>Mortality, No. (%)</td>
<td>0 (0)</td>
<td>12 (57.1)</td>
<td>NS</td>
</tr>
<tr>
<td>All episodes</td>
<td>0 (0)</td>
<td>13 (43.3)</td>
<td></td>
</tr>
</tbody>
</table>

* See Table 2 legend for abbreviation.
† No patients were prescribed prophylaxis prior to 1989. In 1989, 82% of patients were prescribed prophylaxis.

(67% vs 100%; p = 0.091), ICU admission (33% vs 70%; p = 0.252), or overall death (0% vs 43%; p = 0.536), whereas the intubation rate increased significantly from 1985 to 1989, to 1990 to 1995 (0% vs 70%, respectively; p = 0.04)

### Recurrent Episodes of PCP

Table 4 presents the recurrent episodes of PCP and the associated mortality. A total of 241 recurrent episodes of PCP were recorded in the HIV + PCP group. Recurrent episodes of HIV + PCP were not associated with increased mortality up to the fourth episode of pneumonia. In contrast, no recurrent episodes were observed in the non-HIV PCP group.

### One-Year Survival Following ICU Discharges

For HIV + PCP, overall, 36% of patients were alive at 1 year following discharge from the ICU. Comparing the years 1985 to 1989 with years 1990 to 1995, 1-year survival rates were 50% and 26.7%, respectively. In comparison, the overall 1-year survival following ICU discharge for non-HIV PCP patients was 90% (p = 0.0072), and for the periods from 1985 to 1989 and from 1990 to 1995, 1-year survival rates were 100% and 85.7%, respectively.

### Table 4—Mortality Associated With Initial and Recurrent Episodes of PCP

<table>
<thead>
<tr>
<th>Episode of PCP</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-positive patients, No.</td>
<td>364</td>
<td>75</td>
<td>19</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Mortality, No. (%)</td>
<td>39 (11)</td>
<td>13 (17)</td>
<td>4 (21)</td>
<td>1 (17)</td>
<td>1 (50)</td>
</tr>
<tr>
<td>Non-HIV-infected patients, No.</td>
<td>33</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Mortality, No. (%)</td>
<td>13 (39)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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Possible explanations may include the appropriate identification of persons at high clinical risk, the targeted prescription of effective chemoprophylaxis, and more frequent use of empirical treatment for suspected PCP. At this institution, for example, over a period from 1989 to 1993, empirical treatment for PCP increased from 10 to 20% (H. Koziel, MD; unpublished data; October 1996). Although the decline in the incidence of HIV + PCP may reflect the efficacy of HAART controlling viral replication, the observed decline in PCP cases occurred prior to the introduction of potent protease inhibitors, suggesting that other factors contributed to the overall decline in HIV + PCP cases.

The explanation for the increase in non-HIV PCP cases was not specifically addressed in this study. Similar increased incidences have been reported by others. There were no changes in the transplantation programs, changes in the composition or number of non-HIV-infected patients, or changes in the diagnostic approach or management style toward immunosuppressed patients at our institution to account for the observed increased incidence of non-HIV PCP. Possible explanations may include heightened clinical suspicion in the advent of the AIDS epidemic; improved diagnostic techniques, together with increased use of immunosuppressive agents; and expansion of an aging population. Although our understanding of \( P \) carinii epidemiology is limited, increased cases may reflect in part environmental exposures to \( P \) carinii and \( P \) carinii virulence factors (although these are poorly understood).

The decline in hospitalization rates for HIV + PCP may reflect more widespread use of chemoprophylaxis, and improved practice standards as physicians developed experience managing PCP over time, coupled with earlier identification of cases and earlier institution of specific therapy based on a higher clinical index of suspicion. A similar decline in the hospital management of HIV + PCP has been reported by other investigators. The high hospitalization rate for non-HIV PCP may reflect the severity of PCP in this patient population, host response to the organism, underlying immunodeficiency state, advanced age, underlying medical comorbidities, and the more acute presentation for non-HIV PCP.

Respiratory failure was the most frequent indication for ICU admission for both groups, representing 74.4% of HIV + PCP and 95.5% of non-HIV PCP ICU admissions. The overall incidence of acute respiratory failure requiring intubation was much higher in non-HIV PCP cases (63.6%), compared to HIV + PCP cases (5.2%). The higher respiratory failure rate is consistent with published reports and may represent differences in the host-parasite interaction comparing HIV-positive to non-HIV-infected patients, may be related to an influx of neutrophils in the alveolar airspace, or may reflect the underlying medical conditions associated with non-HIV PCP. The high mortality associated with respiratory failure complicating HIV + PCP and non-HIV PCP in the current and other studies clearly highlights the severity of this complication and underscores the need to better understand the pathophysiology to develop new or improved therapeutic interventions.

In the current study, the observed overall mortality for HIV + PCP was 9.6%, similar to that reported by other investigators. In contrast to HIV-infected persons, the overall mortality rate for non-HIV PCP in our study was 39.4%. The poorer outcomes for non-HIV PCP in this study are unlikely due to inexperience in the diagnosis and management of PCP at our institution. Similar high mortality rates reported in other institutions likely in part represent the lack of a standardized approach to the management of non-HIV PCP over the period of this study. The persistently high morbidity and mortality associated with non-HIV PCP observed in the current study suggest that patients with non-HIV PCP have not benefited from the advances in the management of HIV + PCP, although other factors may be important. A recent report comparing HIV + PCP to non-HIV PCP suggests that non-HIV PCP mortality may have decreased since 1995.

For recurrent episodes of HIV + PCP, the mortality rates remain low and relatively stable for up to four episodes, with 79 to 85% survival, similar to report from other centers. Interestingly, no recurrent episodes of non-HIV PCP were identified, which may in part be attributed to the routine administration of specific prophylaxis on recovery from PCP (none of the non-HIV-infected patients were taking prophylaxis at the time of PCP diagnosis), or perhaps to the transient and reversible nature of the underlying immunodeficiency. Recognizing the potential importance of organism burden in AIDS-related PCP, other factors that may influence recurrence rates in the non-HIV-infected population may relate to the relatively low “load” of \( P \) carinii organisms (compared to cases of HIV + PCP).

Other limitations of the current study include the retrospective nature of the investigation, the relative small number of non-HIV PCP cases compared to HIV + PCP cases, and the exclusion of presumptive PCP cases. Although a comparison of experiences of HIV + PCP to non-HIV PCP at a single institution is valuable, the findings at a single institution may not reflect the experience at other institutions with more diverse patient populations. The findings for
HIV + PCP may in part reflect the predominantly homosexual risk group and may not be representative of other HIV risk groups. For the non-HIV PCP cases, the advanced age and the greater proportion of women likely reflect the demographics of persons at risk for acquired immunodeficiency in the absence of HIV infection and are consistent with other reports. Although the study included the period encompassing effective combination antiretroviral therapy, this study did not estimate the impact of newer antiretroviral agents, as the routine prescription of protease inhibitors occurred after 1995. Although the improved HIV + PCP outcomes in the current study were observed prior to the routine use of protease inhibitors, the introduction of HAART may have additional favorable impact on the incidence and outcomes of HIV + PCP.

In summary, this study demonstrates that PCP remains a significant problem in the immunocompromised host and that significant differences remain in PCP outcomes comparing HIV + PCP to non-HIV PCP at our institution. Whereas for HIV + PCP, the annual number of cases, hospitalization, and overall mortality have declined over the period from 1985 to 1995, the number of non-HIV PCP cases has increased, and the need for hospitalization, ICU admission, intubation, and the overall mortality rates remain high. Furthermore, respiratory failure remains a formidable complication associated with high mortality rates for both HIV-infected patients and persons with other immunodeficiency states. This study suggests that whereas improved management and clinical outcomes for HIV + PCP may in part reflect advances in the diagnosis and treatment of this important opportunistic infection, similar benefits have not been apparent for non-HIV PCP. As extrapolation of HIV-related data to cases of non-HIV PCP may not be appropriate, further studies are needed to better identify non-HIV-infected persons at risk, and further define the use of adjunctive agents such as corticosteroids, and to identify and treat patients at risk for respiratory failure complicating PCP.

References

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