More than 50 percent of patients with the acquired immunodeficiency syndrome (AIDS) have involvement of the lungs.\(^1\) The defects in cell-mediated immunity that characterize AIDS predispose to a variety of pulmonary infections caused by pathogens that by and large are considered to be opportunistic.\(^2\) Chief among these is *Pneumocystis carinii* followed by *Mycobacterium avium-intracellulare*, cytomegalovirus, and *Cryptococcus neoformans*. Nonopportunistic organisms such as *M tuberculosis*, *Histoplasma capsulatum*, *Coccidioides immitis*, and *Legionella pneumophila* may also be encountered, although the diagnosis of diseases caused by these agents, even in a patient from a recognized high risk group, does not establish the diagnosis of AIDS. The surveillance definition of AIDS accepted currently by the Centers for Disease Control (CDC) is as follows: the presence of a reliably diagnosed disease at least moderately indicative of underlying cellular immunodeficiency (Kaposi’s sarcoma in a patient less than 60 years of age, *P carinii* pneumonia or other opportunistic infections) occurring in the absence of known causes of underlying immunodeficiency and any other reduced resistance reported to be associated with the disease (immunosuppressive therapy, lymphoreticular malignancy).\(^3\)

As indicated in the definition, Kaposi’s sarcoma is one of the disorders associated with and diagnostic of AIDS. This neoplasm may involve the lungs as well as other viscera, and thus, must be included in a review the pulmonary manifestations of AIDS.

This discussion will review briefly the epidemiologic features and immunologic abnormalities of AIDS and will focus more specifically on the pulmonary diagnostic evaluation of patients with AIDS or suspected AIDS and the management of the lung infections that are encountered frequently. A more comprehensive review of AIDS is found in the report by Fauci and co-workers.\(^4\)

### Epidemiologic Features

#### Incidence

The first published reports concerning AIDS appeared in the summer of 1981.\(^5,6\) Retrospective record reviews identified probable cases as early as 1978, but no earlier. Since the first reports, the total number of cases has increased to nearly 5,000 by the spring of 1984.\(^7\) The number of cases reported has increased each quarter since early in the course of the epidemic and does not show signs of decreasing.

#### Geographic Distribution

Throughout the epidemic, the majority of patients have been from New York City (42 percent), San Francisco (12 percent), Los Angeles (8 percent), Miami (4 percent), and Newark (3 percent). However, cases have been reported from all but eight states and from Canada as well as from at least 20 other countries.

#### Risk Groups

The relative distribution of cases among the groups at risk has remained rather constant since early reports. The groups at greatest risk continue to be homosexual and bisexual men (71 percent), intravenous drug abusers (17 percent), Haitians living in the United States (5 percent), persons with hemophilia (1 percent), heterosexual contacts of persons at increased risk for AIDS (1 percent), and recipients of blood transfusions (1 percent). Approximately 4 percent of patients do not fit into any of the recognized risk groups.

The clustering of cases and the association of the disease with sexual practices and blood products strongly suggest that a transmissible agent with an epidemiologic pattern similar to that of hepatitis B is involved. However, to date, no etiologic agent has been identified in spite of vigorous investigative efforts.

### Immunologic Abnormalities

As the name of the syndrome implies, the most
striking feature of AIDS is immunodeficiency. Although there are functional abnormalities in both T and B lymphocytes, it is the defects in cell-mediated immunity, caused by alterations in T lymphocyte subpopulations, that set the stage for the infectious complications of the syndrome. Characteristically, patients with AIDS have a marked reduction in the ratio of so-called helper T cells to suppressor T cells caused both by an increase in suppressor cells and a decrease in helper cells. In addition, there may be changes in the relative populations of cells within the two subclasses of lymphocytes. Because there is a considerable overlap of helper to suppressor cell ratios between healthy homosexual men and patients with AIDS, and because viral illnesses may cause a transient depression of the H/S ratio, this test cannot be used to establish the diagnosis of AIDS.

Clinically, the defect in cell-mediated immunity is manifested by a failure to react to skin test antigens, such as tuberculin, coccidioidin, histoplasmin, and mumps antigen, that elicit a cell-mediated response. Peripheral blood lymphopenia may also be present, but is quite variable.

The histologic analog of the reduction in cell mediated immunity is the absence of granuloma formation in tissues involved with infection by organisms, such as

\[ M\text{ avium-intracellulare}, \]
that elicit a granulomatous response in persons with normal immunity.* Figure 1 shows acid fast organisms in bone marrow (panel A) and small bowel (panel B). In neither of these tissues is a significant cellular response noted. Also remarkable is the number of organisms present in each of these sites.

Given this profound depression in the ability to fend off pathogens that elicit cell-mediated responses in normal persons, it is not surprising that the infections commonly encountered are with these organisms. It seems likely that the diseases seen represent endogenous reactivation of previously dormant infections. There is substantial evidence that \( P\text{ carinii} \) is acquired as an asymptomatic infection by large numbers of well persons. Similarly, in endemic areas, infection with \( M\text{ avium-intracellulare} \) as evidenced by skin test reactions is highly prevalent. With both of these organisms, there is scant if any evidence of person-to-person transmission, thus favoring the concept of endogenous reactivation. Also favoring this concept is the finding that a high percentage of Haitian entrants to this country who develop AIDS have disseminated tuberculosis as the initial manifestation of the immune defect. This probably relates to the very high prevalence of tuberculous infection among Haitians in general, and therefore, the likelihood that a person developing AIDS will have had prior tuberculous infection.

Presumably, the defect in cellular immunity also is related in some fashion to the development of Kaposi's sarcoma. However, to date, the connection is not clear.

Polyclonal B-cell activation is also a characteristic finding in patients with AIDS. Although there is nonspecific overproduction of immunoglobulins, the ability to mount a specific response to a newly encountered antigen is impaired. These abnormalities of B-cell function have at least two implications that relate to the pulmonary manifestations of AIDS. First, the overproduction of immunoglobulins may be associated with the very high frequency of hypersensitivity reactions to drugs, particularly trimethoprim-sulfamethoxazole, used in treating the pulmonary infections. This may be analogous to the situation that occurs in infectious mononucleosis. Second, although it is not commonly reported, there is the potential for an increased frequency of infections with pathogens that elicit a humoral response.

**Spectrum and Incidence of Pulmonary Complications**

Data presented at a recent National Heart Lung and Blood Institute (NHLBI) workshop on the pulmonary complications of AIDS indicated that of 1,067 patients with AIDS who were evaluated in institutions in New York, Los Angeles, and San Francisco, 441 (41 percent)
Table 1—Pulmonary Involvement in 441 Patients with AIDS*

<table>
<thead>
<tr>
<th>Infections (more than one organism may be present in a single patient)</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>P carinii</td>
<td>373</td>
</tr>
<tr>
<td>M avium-intracellulare</td>
<td>74</td>
</tr>
<tr>
<td>Cytomegalovirus</td>
<td>19</td>
</tr>
<tr>
<td>M tuberculosis</td>
<td>19</td>
</tr>
<tr>
<td>Legionella</td>
<td>19</td>
</tr>
<tr>
<td>Pyogenic bacteria</td>
<td>11</td>
</tr>
<tr>
<td>Cryptococcus neoformans</td>
<td>9</td>
</tr>
<tr>
<td>Other fungi</td>
<td>9</td>
</tr>
<tr>
<td>Herpes simplex</td>
<td>2</td>
</tr>
<tr>
<td>Toxoplasma gondii</td>
<td>1</td>
</tr>
<tr>
<td>Kaposi's sarcoma</td>
<td>36</td>
</tr>
</tbody>
</table>

*From Murray et al.4

had pulmonary complications.2 These disorders and their relative frequencies are listed in Table 1. All 441 patients had at least one opportunistic pulmonary infection and 36 (8 percent) had Kaposi's sarcoma as well. P carinii was, by far, the most common pathogen, being found in 85 percent of patients with pulmonary involvement. These data differ somewhat from those collected by the Centers for Disease Control1 in which P carinii pneumonia alone or coexisting with Kaposi's sarcoma (not necessarily involving the lungs) occurred in 58 percent of patients with AIDS. Thus, a minimum of 58 percent of all reported cases have lung manifestations. In the NHLBI series, other infecting agents with (118) or without (93) P carinii were found in 211 (48 percent) of the 441 patients. Notable for their relative paucity were fungal pathogens that comprised only 1.6 percent of the infecting organisms. Agents which might be expected, such as Aspergillus species, Coccioidoides immitis, and Candida albicans were not encountered. Likewise, nontuberculous mycobacteria other than M avium-intracellulare were not reported, although M scrofulaceum has been isolated from at least two patients. Adenovirus, found in 6 percent of patients in one series, was also not reported in the NHLBI series.15

CLINICAL PRESENTATION

Patients subsequently shown to have AIDS with pulmonary involvement typically have been symptomatic for weeks to months prior to the diagnosis of the pulmonary process. Generally, the symptoms are constitutional and nonspecific including fever, fatigue, and weight loss. Patients who have documented AIDS with Kaposi's sarcoma or nonpulmonary opportunistic infections may present with symptoms dominated by these other processes. Respiratory complaints, predominantly dyspnea and nonproductive cough, usually prompt the evaluation for pulmonary involvement. Additional important information from the history relates to whether or not the patient is from a recognized high risk group, although approximately 4 percent of reported AIDS patients do not fit into any of the groups. It should be noted that the relative distribution among the risk groups varies somewhat from institution to institution depending on the makeup of the community served.

Physical examination may show a somewhat wasted, often febrile patient. Those with more severe pulmonary involvement may be tachypneic. Diffuse lymphadenopathy is often noted. A substantial percentage will have oral candidiasis and a smaller number will have perianal ulcers caused by herpes virus. Findings related to the lungs per se generally are not striking. Dry rales may be heard, but findings indicative of consolidation are unusual.

Initial laboratory evaluation is not particularly helpful. Lymphopenia is common but not invariable. A variety of other hematologic abnormalities including anemia, leukopenia, and thrombocytopenia may also occur. Electrolyte and fluid disorders are uncommon unless the patient has had severe diarrhea.

PULMONARY EVALUATION

Chest Roentgenogram

The chest film is a valuable screening tool. At San Francisco General Hospital in 92 instances of pulmonary involvement with AIDS, comparison of chest films done within one day before lung biopsies and/or bronchoalveolar lavage (BAL) showed only three (3 percent) with totally normal films.16 An additional four

Figure 2. Chest roentgenogram showing fine interstitial infiltration typical of P carinii pneumonia.
patients had normal lung parenchyma, but had other abnormalities (adenopathy, splenomegaly, or pleural fluid) noted; thus, in only 8 percent of instances when lung biopsies and or BAL were diagnostic of pulmonary involvement was the lung parenchyma normal. Not surprisingly, in 50 symptomatic patients with AIDS or suspected AIDS who did not have a specific infection or Kaposi's sarcoma diagnosed, the chest film showed abnormal lung parenchyma in 82 percent and another 8 percent had lymphadenopathy, splenomegaly, or pleural fluid.

The infectious processes with AIDS produced a predominantly interstitial pattern as shown in Figure 2. In interstitial and alveolar pattern, adenopathy and pleural fluid were more common in association with Kaposi's sarcoma (Fig 3). Adenopathy likewise was more common with infections other than \textit{P. carinii} and cytomegalovirus. However, there was sufficient overlap among the roentgenographic findings to preclude making specific diagnoses from chest films alone.

\textit{Pulmonary Function Testing}

Abnormalities in lung function are commonly found in patients who have AIDS with pulmonary involvement. The \textit{P. carinii} pneumonia most consistently causes alterations, although, as with roentgenographic abnormalities, the changes cannot be viewed as specific. Typical findings include reductions in vital capacity (VC) and total lung capacity, increased expiratory flow rates, usually expressed as forced expiratory volume in 1 second over forced vital capacity (FEV/FVC) and a reduced single breath diffusing capacity for carbon monoxide (DCO). Table 2 shows the values for VC, FEV/FVC and DCO in 54 consecutive patients of whom 30 were found to have \textit{P. carinii} pneumonia by lung biopsy or BAL and 24 who also had lung biopsies and BAL and who had other diagnoses or no diagnosis made. As can be seen, there are statistically significant differences in each of these tests between the two groups. With the VC and FEV/FVC, there were substantial overlaps in the values for the two groups; however, no patient subsequently shown to have \textit{P. carinii} pneumonia had a normal (>80 percent of predicted value, corrected for hemoglobin) DCO measurement. Since these data were compiled, we have encountered one patient with \textit{P. carinii} pneumonia who had a normal DCO measurement. Thus, the DCO is highly sensitive, although not specific for the diagnosis of pneumonia caused by \textit{P. carinii}. It should be noted that intravenous drug abuse per se may cause a reduction in DCO as well as abnormalities on chest film, thus occasionally confounding the evaluation of patients in this risk group. 

Arterial blood gas measurements are helpful in determining the severity of pulmonary involvement. Hypoxemia is common but not invariable and hypocarbia may also be seen. Measurement of the alveolar to arterial difference in PaO\(_2\) (P[A-a]O\(_2\)) with exercise seems to be more sensitive than the PaO\(_2\) alone. At least one group has found that there is a significant difference in P(A-a)O\(_2\) with exercise between patients with \textit{P. carinii} pneumonia and those not found to have this infection.

\textit{Gallium Lung Scanning}

Gallium lung scanning has proved to be a very sensitive, although nonspecific, test for the presence of \textit{P. carinii} pneumonia. At San Francisco General Hospital, only one of 22 patients shown to have \textit{P. carinii} on lung biopsy had a normal gallium lung scan. All eight patients with 4+ gallium uptake (uptake greater than that of the liver) had \textit{P. carinii} found in lung biopsy or BAL. Thus, at either end of the scale, 0 or 4+, the gallium lung scan provides diagnostically

\begin{table}[ht]
\centering
\caption{Pulmonary Abnormalities in 54 Patients with and without \textit{P. carinii} Pneumonia}
\begin{tabular}{|c|c|c|}
\hline
 & \textit{P. carinii} & No \textit{P. carinii} \\ (n = 30) & (n = 24) \\
\hline
Vital Capacity (% pred) & 53 (30-95)* & 84 (46-113)† \\
FEV/FVC & 84 (60-98) & 76 (50-99)‡ \\
DCO (% pred) & 55.6 (35-79) & 75 (49-103)† \\
\hline
\end{tabular}
\*Ranges of values.
\†p<0.001.
\‡p<0.05.
\end{table}
useful information. Unfortunately, the intermediate results (1-3+) are nonspecific.

**Transbronchial Lung Biopsy**

There are now ample data attesting to the value of transbronchial lung biopsy in identifying pulmonary infections in patients with AIDS. Transbronchial biopsy performed through a fiberoptic bronchoscope provides a much less invasive means of sampling lung tissue than the traditional open lung biopsy. More important, transbronchial biopsy has a very high yield. In the series from the NHLBI workshop, fiberoptic bronchoscopy with transbronchial biopsy, and in some instances BAL and brush biopsy, yielded 91 percent of the diagnoses of infections. The yield appeared to be higher when transbronchial biopsy and BAL were combined. Identification of an infecting agent by open lung biopsy after a nondiagnostic transbronchial biopsy occurred in ten of 24 patients. Five of seven patients whose initial bronchoscopic procedures were nondiagnostic had repeat transbronchial biopsies that identified infecting organisms. Thus, of 31 patients whose initial bronchoscopies did not provide a diagnosis, a second procedure, either open lung biopsy or transbronchial biopsy, identified pathogens in 15.

In contrast, transbronchial biopsy is very insensitive in making the diagnosis of Kaposi's sarcoma in the lung. The therapeutic implications of this finding, however, are very limited. Thus, once infection is excluded, making the diagnosis of Kaposi's sarcoma involving the lung is not of great importance.

We routinely perform fiberoptic bronchoscopy with transbronchial biopsy via a transnasal approach without an endotracheal tube. Unless there is a focal abnormality, the procedure is done "blindly," that is, without fluoroscopic guidance. This saves time and cost to the hospital and the patient. We attempt to obtain six pieces of tissue with each procedure.

The complications of transbronchial biopsy consist mainly of hemorrhage and pneumothorax. In our series of 124 consecutive transbronchial biopsies in patients with AIDS or suspected AIDS, pneumothorax occurred in 7.7 percent with six of these (4.6 percent the total procedures) requiring placement of a chest tube for re-expansion. Hemoptysis sufficient to cause respiratory compromise or to necessitate blood transfusion did not occur, and there was no death. The presence of an uncorrectable coagulopathy is an absolute contraindication for transbronchial biopsy. Respiratory failure sufficiently severe to require mechanical ventilation is a relative contraindication to transbronchial biopsy because of the high likelihood of tension pneumothorax. If transbronchial biopsy is performed in a patient who is being mechanically ventilated, a chest tube should be immediately available or perhaps placed prior to the procedure.

<table>
<thead>
<tr>
<th>Table 3—Examination of Bronchoscopically-Derived Specimens in Patients with AIDS or Suspected AIDS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Transbronchial Biopsy</strong></td>
</tr>
<tr>
<td>Touch imprints (Giemsa, Gram-Weigert, Wright-Giemsa or modified Grocott stains)</td>
</tr>
<tr>
<td>Fixed tissue sections (hematoxylin-eosin, methamine silver, acid fast and fungal stains, immunofluorescence for Legionella)</td>
</tr>
<tr>
<td>Culture for mycobacteria, pyogenic organisms, fungi, viruses</td>
</tr>
<tr>
<td><strong>Bronchoalveolar Lavage Fluid</strong></td>
</tr>
<tr>
<td>Same as above with exception of fixed tissue sections. Pellet from centrifuged fluid is stained instead of tissue.</td>
</tr>
</tbody>
</table>

The routine examination of tissue specimens is summarized in Table 3. These procedures should identify the vast majority of known pathogens. The use of touch imprints made from tissue specimens and stained with Giemsa, Wright-Giemsa, or Gram-Weigert stains is a very sensitive means of detecting *P. carinii* and has the advantage of being rapid, as opposed to the slower methamine silver staining of fixed tissue sections.

Routine tissue histopathology with hematoxylin-eosin staining has not proved to be particularly useful except perhaps in the diagnosis of pneumonitis caused by cytomegalovirus. Patients with AIDS seem incapable of forming granulomas in response to mycobacterial or fungal infections, and thus, the absence of this histologic finding does not exclude diseases caused by these organisms. In addition, routine cytologic examination of specimens obtained by brush biopsy is not helpful unless a specific visible lesion is brushed.

**Bronchoalveolar Lavage**

Bronchoalveolar lavage is most commonly performed through a fiberoptic bronchoscope, although balloon-tipped, double lumen catheters can also be used. The yield of infectious diagnoses from BAL alone is quite high. Broadus and co-workers have reported an overall yield of 90 percent for infecting pathogens in 106 instances where both BAL and transbronchial biopsy were performed. The *P. carinii* was detected in BAL fluid of 89 percent (58 of 65) patients proven to have pneumocystosis. Lavage fluid was positive in four instances in which the organisms were not seen in tissue specimens.

Bronchoalveolar lavage is performed by positioning the bronchoscope in a peripheral airway and instilling 100 to 140 ml of fluid in 20 ml aliquots. The aspirated return is usually 50 to 70 ml. The fluid is processed much as outlined for tissue with staining of a pellet of cells obtained by centrifugation for *P. carinii*.

The advantage of BAL over transbronchial biopsy is the much lower frequency of complications. Because tissue is not sampled, hemorrhage and pneumothorax do not occur; thus, the procedure can be performed in patients with coagulopathies or who are being mechan-
PATIENT FROM RISK GROUP OR KNOWN AIDS

**RESPIRATORY SYMPTOMS**

- Abnormal lung parenchyma
- Coagulation Tests
- Arterial Blood Gas Measurements
- Normal Lung parenchyma
- Pulmonary Function Tests
- Abnormal DLCO
- Gallium Scan
- Abnormal Bronchoscopy (Lavage and Biopsy)*

**CHEST FILM**

- Satisfactory Coagulation
- Satisfactory Gas Exchange
- Bronchoscopy (Lavage & Biopsy)
  - No diagnosis
  - Diagnosis
  - Treatment
- Lavage
  - No further evaluation
  - Observation or repeat bronchoscopy
  - Repeat bronchoscopy or open lung biopsy

* Biopsy performed if contraindication not present

**Figure 4.** Sequence of diagnostic evaluations in patients suspected of having pulmonary involvement with AIDS.

...clinically ventilated. The only complications are introduction of a new infection and possibly worsening gas exchange because of the volume of fluid instilled.

**Open Lung Biopsy**

Open lung biopsy in patients with AIDS should be reserved for several situations that are encountered infrequently as follows: (1) a patient with progressive pulmonary disease in whom a carefully performed fiberoptic bronchoscopy with BAL and transbronchial biopsy were nondiagnostic. Even in this situation, a second bronchoscopic procedure may be indicated prior to open lung biopsy. If possible, one should wait until the results of all microbiologic evaluations of the initial specimens have been returned; (2) a patient with an uncorrectable coagulopathy in whom BAL has been nondiagnostic; (3) a patient who is requiring mechanical ventilation in whom biopsy or BAL has been nondiagnostic.

**Summary**

Utilizing the information presented above, a logical plan for the pulmonary evaluation of AIDS or suspected AIDS patients can be developed. The diagnostic approach is summarized in Figure 4.

**TREATMENT**

Treatment of pulmonary involvement in patients with AIDS is determined by the specific disorder that is diagnosed. There is general agreement that empiric therapy should not be undertaken except, perhaps, for short periods of time while diagnostic procedures are being arranged or specimens are being processed.

**P carinii Pneumonia**

The most commonly encountered of the opportunistic infections in patients with AIDS is also one of the most responsive to treatment. Two drugs, trimethoprim-sulfamethoxazole (TMP-SMX) and pentamidine isethionate have been used for a number of years to treat this disorder. Based on reviews of the results of therapy in patients having more conventional forms of immunosuppression, TMP-SMX appeared to be the more effective agent with response rates in the range of 85 percent when the drug was given for more than nine days. The rate of response in patients given pentamidine for more than nine days was approximately 65 percent. In addition, there was a greater frequency of adverse effects caused by pentamidine than TMP-SMX. Thus, in the pre-AIDS era, TMP-SMX was clearly the drug of choice for P carinii pneumonia. In patients with AIDS, however, both prospective and retrospective evaluations of the two agents do not show this clear superiority of TMP-SMX. In a retrospective evaluation of treatment for P carinii pneumonia in patients with AIDS, Gordin and co-workers found that of 37 patients treated with TMP-SMX, two patients died within seven days and 11 were changed to pentamidine because of failure to respond. In 19 patients, adverse reactions necessitated changing from TMP-SMX to pentamidine. Thus, only five (14 percent) completed treatment with TMP-SMX successfully. The kinds of adverse reactions and the frequency with which they occurred are shown in Table 4.

A prospective comparison of TMP-SMX and pentamidine with patients assigned at random to either drug, confirmed the results of the retrospective review.
Table 4—Adverse Reactions to TMP-SMX and Pentamidine in 36 Patients with AIDS and P. carinii Pneumonia*

<table>
<thead>
<tr>
<th></th>
<th>TMP-SMX (n = 35)</th>
<th>Pentamidine (n = 30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rash</td>
<td>12</td>
<td>1</td>
</tr>
<tr>
<td>Fever</td>
<td>13</td>
<td>1</td>
</tr>
<tr>
<td>Leukopenia</td>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Azotemia</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Hepatitis</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Any reaction</td>
<td>23</td>
<td>7</td>
</tr>
</tbody>
</table>

*From Gordin et al. All but seven patients received both drugs.

with regard to the frequency of adverse reactions to TMP-SMX. In addition, however, the data showed a similar frequency of adverse reactions to pentamidine. Rates of success were nearly equal for the two drugs.

In the NHLBI workshop series, 133 (72 percent) of 185 patients initially treated with TMP-SMX for first episodes of *P. carinii* pneumonia survived. Of 33 patients who failed to respond to TMP-SMX and were switched to pentamidine, 88 percent (29) died, whereas all 41 patients who were switched to pentamidine because of adverse reactions to TMP-SMX survived. Thus, 48 percent (88) of the original 185 patients completed treatment with TMP-SMX successfully. The reasons for the lower frequency of adverse effects to TMP-SMX in the NHLBI series compared to both the retrospective and prospective studies cited previously are not clear, although the mean duration of treatment was shorter in the former group and may account for some difference.

Based on available data, in patients with AIDS, neither TMP-SMX or pentamidine is clearly superior for first episodes of *P. carinii*. There are, however, certain instances in which one or the other would be desirable. The TMP-SMX is probably preferable in patients with pre-existing renal failure. In patients with coagulation disorders, pentamidine, which is generally given intramuscularly, cannot be given via that route. Patients who require restriction of fluid intake should be started on pentamidine because intravenous administration of TMP-SMX requires a minimum of 1,200 ml of 5 percent dextrose in water daily. Pentamidine is probably preferable to TMP-SMX in patients with pretreatment leukopenia or anemia, although pentamidine, like TMP-SMX, may cause marrow suppression or neutropenia. Pentamidine is also the drug of choice in patients who have a history of prior allergic reactions to TMP-SMX or other sulfa drugs. Severe hypersensitivity reactions may occur in this group if rechallenged with TMP-SMX.

The usual dose of TMP-SMX is 20 mg/kg of the TMP component and 100 mg/kg of the SMX daily, divided into four doses given intravenously for a minimum of 14 to 21 days. Patients should be hospitalized for the duration of their treatment. Complete blood counts, platelet counts, and tests of renal and hepatic function should be obtained at three-day intervals. Progressive leukopenia, usually neutropenia, to a total white blood cell count of less than 2,000/µl or an absolute neutrophil count of less than 1,000/µl, thrombocytopenia (less than 50,000/µl), or progressive alterations in renal or hepatic function are indications for changing to pentamidine. Severe skin rashes and significant drug fever may also necessitate changing treatment.

Pentamidine isethionate is given in a single daily dose of 4 mg/kg. It is recommended that the drug be given intramuscularly; however, we have considerable experience with intravenous administration and feel that this can be safely carried out if the dose is given in 250 ml of 5 percent dextrose in water over a two to three hour period with careful checking of arterial blood pressure. The serious early side effects of pentamidine are hypotension and hypoglycemia. Intramuscular administration may cause sterile abscesses. In addition, as with TMP-SMX, neutropenia, impairment of renal function, and hepatitis may occur. Skin rashes and drug fever seem less common than with TMP-SMX.

With either drug, demonstrable clinical improvement should not be expected until after a minimum of three days of treatment. If by day 4 improvement is not seen, especially in a patient with severe gas exchange abnormalities, consideration should be given to changing agents. It should be kept in mind that this situation is associated with a very poor prognosis.

The course of the treated disease is quite variable. An illness that has progressed rapidly prior to institution of therapy tends to be associated with a poor response to treatment and a bad prognosis. The survival rate for patients who required mechanical ventilation in the NHLBI series was only 14 percent and in our own experience is less. Patients with a more indolent course do much better, generally showing improvement in chest films and pulmonary function studies as well as symptoms. However, follow-up bronchoscopic examination with BAL and transbronchial biopsy after 21 days of therapy showed *P. carinii* in 16 of 24 patients at San Francisco General Hospital. The meaning of this finding is not clear at present.

There is very little experience with using TMP-SMX as a preventive agent in persons in high risk groups or in patients who have completed therapy for *P. carinii* pneumonia. Given the frequency of side effects from the drug, however, preventive therapy does not seem justified. Also, perhaps surprisingly, the rate of relapse seems low in patients who complete treatment successfully.
These same basic guidelines apply to the management of second episodes of *P. carinii* pneumonia, although the rate of successful treatment is substantially less (seven of 20 in the NHLBI series).

**M. avium-intracellulare**

The management of pulmonary disease caused by *M. avium-intracellulare* is difficult in nonimmunocompromised patients because of the resistance of the organism to antimicrobial agents. Even with aggressive medical therapy, overall success rates are in the range of 45 percent to 65 percent.59,67 The situation is much more difficult in patients with AIDS in whom the process is commonly disseminated with the organism being isolated from bone, lung, marrow, and other tissues in addition to the lungs. Moreover, disease from *M. avium-intracellulare* often seems to be a “second wave” of infection in persons who are more severely affected by the syndrome. Given these considerations, it is not surprising that this disorder is particularly difficult to treat in patients with AIDS. Standard antituberculosis agents in combinations of three to five drugs seem to have little effect. These drugs combined with ansamycin (LM 427), a rifamycin derivative, and clofazamine, an antileprosy compound, seem to have a better rate of clinical response.68,69 However, assessment of effect is difficult because of the multiplicity of illnesses in these patients and the need for invasive procedures to document bacteriologic cure. As with the drugs used to treat *P. carinii*, adverse reactions to the drugs used to treat *M. avium-intracellulare* are common. Broadly applicable guidelines for the treatment of this infection cannot be provided at this time.

**Fungi**

The general principles of management of fungal infections in nonimmunocompromised patients apply in their treatment in patients with AIDS. Amphotericin B, beginning with doses of 0.25 mg/kg/day, and increasing to 0.5 mg/kg/day for a minimum of six weeks, represents standard treatment.

**Other Infections**

Pneumonia caused by *Legionella* species should be treated with erythromycin, 500 mg to 1 g, four times a day for a total of three weeks. Tuberculosis is treated using standard drug regimens containing isoniazid, rifampin, and ethambutol. At present, there is no treatment for cytomegalovirus pneumonia.

**Kaposi’s Sarcoma**

Approaches to management of Kaposi’s sarcoma involving the lungs are no different than management of the tumor when it involves other organs.68 A possible exception to this, however, is the management of pleural effusion caused by pleural involvement. In this situation, chest tube drainage and pleural sclerosis may be necessary.

**Prognosis**

In spite of the general effectiveness of treatment for *P. carinii* pneumonia, the most frequent pulmonary complication of AIDS, the ultimate prognosis is not changed. Median survival time for patients with opportunistic infections is 6.4 months with a nearly 100 percent mortality rate by 24 months. For patients with Kaposi’s sarcoma only (not necessarily involving the lungs), median survival is 16.7 months with approximately 25 percent survival at two years (Centers for Disease Control, personal communication). Thus, although treatment of the pulmonary complications probably prolongs life and improves its quality, the eventual outcome is the same as if the infection were not treated. For this reason, it is essential that the vigor of diagnostic and treatment efforts be balanced against the short-term goals of improving quality of life and maintenance of patient comfort. Patients should be fully apprised of the situation and incorporated in a meaningful way into the decision making process. This is particularly the case with decisions concerning mechanical ventilation and other means of life support. Patient counselling and social and psychological support are essential parts of any treatment program.

**Infection Control**

Rational approaches to infection control are difficult to define because of the lack of knowledge concerning the etiology of AIDS. However, the parallels between the epidemiologic patterns of AIDS and hepatitis B enable some guidelines to be developed.67 The potential hazards are perhaps greatest in performing bronchoscopy where contact with oral and respiratory tract secretions and often blood is unavoidable. Persons involved in performing the procedure should wear water impermeable gowns and gloves. In addition, to prevent oral, nasal, or ocular mucous membrane contact with secretions, masks and protective eyewear should be worn. Bronchoscopes and reusable instruments should be thoroughly cleaned and gas sterilized after each use. Tissue specimens and lavage fluid should be handled as is recommended for blood specimens and placed in closable plastic bags with hazard labels affixed.

The main concern with pulmonary function testing equipment is contamination by saliva. For this reason, disposable mouthpieces should be used. Persons drawing arterial blood specimens should wear gloves and be careful not to contaminate environmental surfaces. The specimens themselves should be placed in plastic bags for transport.

Patients who are being mechanically ventilated are a particular concern in that commonly, there is heavy
environmental contamination with blood, and oral and
respiratory tract secretions. Gloves should be worn by
persons who will be in contact with the patient and his/
her bedclothing. Gowns should be worn by staff who
have repeated or prolonged contact. If tuberculosis has
not been excluded, appropriate precautions should be
employed against airborne transmission of infection.
Because of the concern with cytomegalovirus as a
cause of fetal abnormalities, pregnant women should
not be involved in the care of patients with AIDS or
suspected AIDS.

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