PULMONARY FUNCTION TESTS IN NONINFECTIOUS DISEASES

An emphasis on infectious causes of respiratory signs and symptoms is justified since infections account for 40% to 75% of the pulmonary complications in immunosuppressed patients, and mortality may approach 50% without early recognition and treatment.[109] Recognition of the noninfectious causes is equally important to provide more accurate prognosis and management, and to avoid or limit the use of potentially toxic antimicrobials.

Noninfectious pulmonary diseases vary widely in different immunosuppressed populations. Diffuse pulmonary infiltrates are a common radiographic finding; the differential diagnosis includes over 130 different syndromes.[110] In the immunosuppressed host, infections and idiopathic interstitial pneumonia are most common. Pulmonary edema is common in renal transplant patients or the older immunosuppressed patient, while septic patients may develop noncardiogenic pulmonary edema or ARDS. Lung metastases, pulmonary hemorrhage, drug reactions, and radiation injury are common in oncology patients. The predominant PFT abnormalities associated with these commonly encountered but diverse pulmonary complications are summarized in Table 12-2 and discussed in more detail below.

Cardiogenic Pulmonary Edema and ARDS

The immunosuppressed host is at increased risk for pulmonary edema due to impaired cardiac or renal function. In renal transplant patients, 12% of pulmonary complications are due to pulmonary edema.[109] Diminished cardiac reserve caused by chemotherapeutic agents and compounded by intravascular volume loading will often result in pulmonary edema. Weight changes, cardiac examination, radiographic appearance, and response to diuretics are of primary diagnostic importance. Early, subtle degrees of congestive heart failure may be associated with mild reductions in VC and an elevated DLco due to dilation of pulmonary capillary bed; a high DLco/VA ratio is consistent with the diagnosis of pulmonary congestion. As alveolar edema progresses, DLco and VA also decrease and the DLco/VA ratio may approach normal or even decrease. In contrast, diffuse infiltrates due to ARDS or interstitial pneumonias are characterized by a greater decrease in DLco, resulting in a decrease in the DLco/VA ratio. Peripheral airway obstruction, detected only from a concave flow–volume loop (see Fig. 12-2,D), can be expected, in part due to edema fluid surrounding the peripheral airways.

Most commonly, edema occurs in the severely ill hospitalized patient with cardiovascular decompensation or conditions that predispose to noncar-

Table 12-2. Pulmonary Function Tests in Immunosuppressed Patients with Pulmonary Diseases

Disease	VC	FEV_1/FVC	TLC or VA	DLco	DLco/VA	O_2 Rest	O_2 Exercise	CO_2
P. carinii pneumonia, viral pneumonia, or ARDS	↓ ↓	↑ (20% ↓)	↓	↓ ↓ ↓	↓	↓	↓ ↓ ↓	↓
Thromboembolism	→ (↓)	→ (↓)	→ (↓)	↓ ↓ ↓	↓ ↓	↓	↓ ↓	↓
Drug reactions, radiation-induced pneumonitis, LIP, IIP	↓	↑	↓	↓ ↓	↓	↑ (↓)	↓ ↓	↓
Bacterial pneumonia	↓	↓ ↓	↓	↓	→	↓	↓	→ (↑)
Bronchiolitis obliterans	↓ ↓	↓ ↓ ↓	↑	↓ ↓	→	↓	↓ ↓	→ (↑)
Tuberculosis fungi	↓	↓	↓	↓				
Mediastinal or endobronchial carcinoma		—			→	→	→	→
Cardiogenic pulmonary edema	↓ (↓ ↓)	↑ (↓)	↓	↑ (↓)	↑	→ (↓)	↓ ↓	↓
Pulmonary hemorrhage	→ (↓)	→	→ (↓)	↑ ↑	↑ ↑	→	↓	↓

Notes: Arrows indicate the direction of change and, in general, the severity, frequency, and selectivity of a test for a typical moderately advanced case of the disease. Horizontal arrows (→) indicate normal values. Symbols in parentheses indicate more severe or unusual manifestations of the disease group. An underscore denotes the most characteristic PFT for that group. LIP = lymphocytic interstitial pneumonitis, IIP = idiopathic interstitial pneumonitis, VC = vital capacity, FEV_1/FVC = ratio of forced expiratory volume in 1 second to forced vital capacity, TLC = total lung capacity, VA = alveolar volume, DLco = lung diffusing capacity.

diogenic edema or ARDS. These conditions are discussed in detail in other chapters; respiratory monitoring is emphasized here. The respiratory rate is perhaps the easiest of lung function tests to perform and the one that best correlates with the work of breathing and hypoxemia.[71] Incentive spirometry not only monitors the VC but also may help prevent the progression of atelectasis, a major early cause of impaired gas exchange. A respiratory rate in excess of 30/min or a VC less than 1 L precedes respiratory failure and mandates arterial blood gas measurements or monitoring with pulse oximetry.[8,29,71] However, oximetry may be erroneous and misleading when hemodynamic and peripheral perfusion are compromised, as is frequent when pulmonary edema is present. Therefore, arterial blood gas measurements are the most useful way to monitor lung infection in the setting of acute, severe pulmonary edema.

Despite extensive alveolar damage and even fibrosis associated with ARDS, in those who survive, full recovery of pulmonary function can be expected in the nonimmunosuppressed host.[71,72,111] Remodeling of lung parenchyma with transition of type 2 cells to type 1 alveolar lung cells may extend over many months, as demonstrated by the slow recovery of DLco.[71,111] About 25% of patients are left with obstructive or hyperreactive airways disease.[72]

Malignancy

The lung in malignant disease can exhibit a wide range of pathology and pulmonary function abnormalities. Space-occupying parenchymal lesions may be primary or metastatic: the lung is second only to bone as the most common site of spread of cancer. Endobronchial invasion can cause segmental or lobar atelectasis or postobstructive pneumonia, while more proximal lesions can cause fixed intrathoracic or extrathoracic obstructive patterns in the flow–volume loop (see Fig. 12-2,F). Mediastinal and hilar involvement also cause similar large airway obstruction patterns and, in addition, cause vascular obstruction and perfusion defects suggesting pulmonary emboli. Leukemic infiltrates occur in 30% of leukemia patients and manifest with an interstitial pattern on radiographs[112,113]; lymphangitic carcinoma presents similarly. These may clinically and physiologically resemble interstitial pneumonia or even ARDS with a decrease in DLco and hypoxemia. Lymphatic obstruction or direct pleural involvement causes pleural effusion which reduces lung volume with or without interference with gas exchange. The VC can be a useful guide to the need for repeat thoracentesis.

Lymphoma. In Hodgkin's lymphoma, mediastinal adenopathy occurs in 40% to 50% of patients, while parenchymal disease is present in 15% to 40%.[114,115] Even in non-Hodgkin's lymphoma up to 30% of patients have chest involvement.[116] The most common pulmonary presentation is bronchial obstruction with volume loss, particularly if associated with lobar atelectasis or pneumonitis.[117] Since therapy frequently involves radiation or drugs that affect lung function, baseline determinations of volumes and DLco may be invaluable in later assessments.

Leukemia. Though over 30% of patients with leukemia may have parenchymal infiltrates,[118,119] most of these patients are asymptomatic and have normal chest radiographs.[120,121] As in lymphoma, hilar, mediastinal, and pleural involvement is common. Chronic lymphocytic and myelogenous leukemia are associated with pleural effusions and volume loss. In later stages of acute leukemia, patients may present with a syndrome similar to ARDS—severe hypoxemia generally associated with high blast counts—and improve with chemotherapy.[120] Conversely, an ARDS-like illness can occur acutely after chemotherapy, presumably owing to release of toxic products from lysed cells.[121] There is little in the literature relevant to lung function in these patients. Baseline and serial studies of volume and DLco should be of value, particularly if chemotherapy and the use of cytotoxic drugs such as bleomycin are contemplated, as discussed below.

Kaposi's Sarcoma. In AIDS patients, Kaposi's sarcoma accounts for 9% of pulmonary complications.[34] Mucosal invasion by Kaposi's sarcoma is common. Endobronchial lesions can cause fixed extrathoracic airway obstruction which may produce a plateaued flow–volume loop (see Fig. 12-2,F). Airway obstruction was reported in 12 patients with Kaposi's sarcoma and endobronchial lesions.[59,60] Airway obstruction without endobronchial lesions has also been reported in AIDS patients with and without Kaposi's sarcoma, but the cause is unclear.[59,60]

Lymphatic Kaposi's sarcoma can involve the lungs and pleura and result in loss of volume and DLco. It is not common for pulmonary involvement to predominate without visible mucosal lesions. Our experience suggests that the pulmonary function abnormalities correlate with the radiographic severity, with a concomitant and slow decline in VC and DLco (see Fig. 12-4,C). A decrease in DLco without obvious lesions on the chest radiograph would more likely be explained by conditions other than Kaposi's sarcoma. When busulfan is given therapeutically in doses exceeding 100 units, a decline in DLco is expected, perhaps in all patients.[122]

Pulmonary Hemorrhage

Intraalveolar or interstitial hemorrhage may be an underdiagnosed problem in immunosuppressed patients with thrombocytopenia. It was reported in 9 of 12 such patients, based on the finding of hemosiderin-laden alveolar macrophages obtained from BAL.[123] Pulmonary hemorrhage was found in 62% of leukemia patients at autopsy; in 38% of these patients, pulmonary hemorrhage was considered the cause of the pulmonary infiltrate.[124] Since the intraalveolar hemoglobin absorbs CO, the DLco will increase with hemorrhage and has been found to correlate with the radiolographic findings.[125] Serial DLco measurements have been suggested as a way to monitor pulmonary hemorrhage in active Goodpasture's disease.[126] The combination of stable or rising DLco and the presence of hemosiderin-laden macrophages recovered from BAL fluid in a patient with thrombocytopenia or other cause of hemorrhagic diathesis should suggest pulmonary hemorrhage as the cause for radiolographic infiltrates.

Thromboembolism

Coagulation disturbances are common, particularly in immunosuppressed patients with malignancy. Prolonged periods of immobilization, major surgery, age, and congestive heart failure all predispose to deep venous thrombosis and thromboembolism. Characteristically the patient is febrile and dyspneic, DLco and Pa_{O_2} are depressed, lung volumes exhibit little or no change and the chest radiograph is normal. *P. carinii* or viral pneumonia may have a similar presentation. Fever and focal infiltrates due to atelectasis or infarction from pulmonary embolism mimic pneumonia or tumor. It has been reported that a high V_D may be diagnostic, but this too is nonspecific.[127] If thromboembolism is suspected, one should look for deep veinous thromboembolism by venous imaging of lower extremities, or pulmonary embolism by ventilation/perfusion scan, particularly when the chest radiograph is clear.

Interstitial Pneumonitis

Although there are approximately 130 defined interstitial lung diseases, noninfectious interstitial pneumonitis is generally idiopathic, with a cause known in only 25% to 30% of cases.[110] In the immunosuppressed host it is usually a nonspecific idiopathic or lymphocytic interstitial pneumonitis that is described.[128,129]

In a recent study by Ognibene and colleagues at NIH,[68] idiopathic interstitial pneumonitis was found by transbronchial biopsy in 11 of 23 HIV-infected patients with T4 counts of less than 200 mm^3 and without pulmonary symptoms when the chest radiograph was clear. No *Pneumocystis* was found, disproving their original hypothesis that silent colonization with *Pneumocystis* might account for the frequency of *P. carinii* pneumonia. This same group had earlier reported that 42 of 152 episodes of pneumonitis in AIDS patients were idiopathic interstitial pneumonitis.[129]

Idiopathic interstitial pneumonitis is extraordinarily common in bone marrow transplant recipients. In a nine-year experience at Johns Hopkins, 166 episodes of interstitial pneumonia were recorded in 386 consecutive bone marrow transplant patients; 57 were idiopathic, 53 were of "unknown" cause, 41 were due to CMV, and only 6 were due to *P. carinii* pneumonia.[39] Though CMV and *P. carinii* pneumonia have diminished with effective prophylaxis, idiopathic interstitial pneumonitis remains a high risk, occurring in 15% to 20% of all bone marrow transplant patients and in over 40% of patients receiving chemotherapy or total body radiation therapy, or with graft-vs-host disease.[39]

A viral etiology of idiopathic interstitial pneumonitis has been suspected, as the cellular response in early disease is similar to that seen in viral pneumonia.[130] Lymphocytic interstitial pneumonia has been described in children of AIDS mothers[131] and in association with Epstein–Barr virus[132] and elevated titers of HIV-specific antigen,[133] all suggesting a viral-induced immunologic reaction. It is not suprising, then, that the pulmonary function changes are similar to those described with viral pneumonias.

Characteristically, the lung volumes may be normal early in the disease while the DLco deteriorates earlier and more dramatically than VC and TLC.[134,135] Resting $P_{A-a_{O_2}}$ is increased and correlates with DLco below 60%.[21] Ventilation/perfusion abnormalities are most severe during exercise, as demonstrated by the rise in $P_{A-a_{O_2}}$ and V_D.[135–139] Generally, the flows and FEV_1/FVC ratio are high, as is characteristic of decreased elastic recoil associated with interstitial disease,[140] but small airways disease may also be present, with decreased flows at low lung volumes and concavity demonstrated on the flow–volume curve.[141]

It is clear from the 1978 studies in non-AIDS idiopathic interstitial pneumonitis by Epler and colleagues[142] as well as the 1988 report by Ognibene *et al*[68] that chest radiographs can be normal in patients with significant functional abnormalities. Although only 4 of the 11 with idiopathic interstitial pneumonitis reported by Ognibene *et al*[68] had DLco values below 80%, 7 of the remaining 13 with no pathology on biopsy had DLco values below 80%.

In addition, positive gallium uptake was present in 7 of 11 with idiopathic interstitial pneumonitis and in 4 with no pathology but with low DLco values (43% to 67% of predicted), suggesting that significant pathology was present but was missed by sampling error of transbronchial biopsies. Gallium scan was normal in 4 of the 11 patients with idiopathic interstitial pneumonitis,[68] as has been reported even in patients with clinical and functional abnormalities.[143]

Though PFT changes frequently do not correlate with the pathology,[68,144] they are most useful for prognosis and guiding management. Clinical deterioration is not related to chest radiographic changes or immunologic test results but is related to declines in P_A–aO_2, VC, and DLco.[145,146] Improved pulmonary function will also correlate with the response to steroids or other immune-suppressing treatments.[147] In 56 patients with idiopathic interstitial pneumonitis followed for up to 19 years, nonsurvival was predicted if the VC was less than 60% and the DLco was less than 40%.[148]

In the AIDS population, idiopathic interstitial pneumonitis generally is not a progressive condition.[68] When serial DLco or exercise P_A–aO_2 values deteriorate, other causes should be sought. Lymphocytic interstitial pneumonitis, on the other hand, is a more active disease process but does respond to steroids.[39] Monitoring VC and DLco provides a guide to inititate or optimize steroid treatment, which has the potential to aggravate the primary immune deficiency and increase the risk for opportunistic infection.[149]

Radiation-Induced Pneumonitis

Radiation therapy can produce a wide range of pulmonary reactions. Radiation-induced pneumonitis is generally divided into an acute phase (one to three months), a latent phase (three to six months), and a fibrotic phase (six to 18 months). In the acute phase, there may be congestion, hypoxemia, and lymphangiectasia,[150] as well as necrosis of broncheolar epithelium[151] and thrombosis.[152] Thus, increased airway reactivity (bronchospasm), restriction, and diffusion defects may be found early during treatment.

The "latent phase" may be a misnomer, as there may be a mononuclear alveolitis[153,154] that contributes to the progressive pulmonary and pleural fibrosis evidenced in the chronic phase with radiologic infiltrates and declines in VC and DLco.[155] Hypoxemia, particularly with exercise, can also be expected.[156]

The frequency of significant radiation-induced pneumonitis is low. Only 12 of 234 patients with pulmonary radiation exposure were found to have this condition.[157] Current estimates are that 5% to 15% will have clinical disease, but few will die of it.[158,159]

There is speculation that in some cases, nonpulmonary radiation therapy or unilateral pulmonary radiation therapy can initiate a systemic response that results in diffuse or contralateral pulmonary injury.[160] Again, restriction, diffusion defects, and impaired oxygenation are characteristic. Baseline pulmonary function studies and awareness of such reactions with early measurements may indicate the need for supplemental oxygen and steroid treatment[160] before radiologic features are evident.

Bronchiolitis Obliterans and Graft-vs-Host Disease

There are several reports of obstructive airways disease occurring 6 to 12 months after bone marrow transplantation; there is a strong correlation with graft-vs-host disease.[161–163] Acute graft-vs-host disease develops in 25% to 75% of bone marrow transplant patients, followed by chronic graft-vs-host disease.[164] Obstructive airways disease has been noted in 20% of those with graft-vs-host disease one year after bone marrow transplantation[163]; some had preexisting obstructive airways disease, but 11% showed a greater than 15% decrease in the FEV_1/FVC ratio. Others have reported a 13% incidence of obstructive airways disease.[165] Lymphocytic bronchitis is found at autopsy in 25% of bone marrow transplant patients. These findings may in part relate to the pretransplant chemotherapy, infections, and drug reactions, but the histologic picture of bronchiolitis obliterans has been repeatedly confirmed.[163]

A similar disorder is reported in 10 of 20 long-term survivors of heart–lung transplants.[38] In these patients it is postulated that the airways disease is a manifestation of graft rejection, though the disease occurs in a setting unrelated to rejection.[38] A more recent study showed that the rate of decline in FEV_1 and midexpiratory flow rates in heart–lung transplant recipients was markedly slowed by augmented immunosuppression.[166] This study represents a logical use of serial PFTs in the immunosuppressed host.

The spectrum of bronchiolitis obliterans associated with organizing pneumonia in 50 cases without identified causes was described by Risk *et al.*[22] The patients usually had had "flu-like illness" in the preceding three to ten weeks. Physiologically, obstructive airways disease was limited to smokers, restriction was present in 72%, and diffusion was impaired in 86%. This series included no immunosuppressed patients, and clinical and physio-

logic recovery occurred in 65% after treatment with steroids. In another series, also not involving immunosuppressed patients, 80% responded to steroids.[167] The response in the bone marrow and heart–lung transplant patients was poor. However, two of ten heart–lung transplant patients who were treated with high-dose steroids[38] when the disease was first detected did improve, suggesting that careful monitoring for peripheral airway obstruction and for declines in VC and DLco may allow institution of earlier and more effective treatment.

Drug Reactions

The wide spectrum of drug-induced diseases is well described.[168,169] Drug-induced pulmonary diseases can be severe, even fatal, yet they are difficult to diagnose as the findings mimic other diseases in immunosuppressed patients such as infections or the underlying malignancy for which the drug was originally prescribed. Reactions are amplified when associated with radiation therapy or high oxygen concentrations, which may produce similar pathologic and physiologic changes (see Table 12-2).

The most common, serious drug-induced lung diseases in immunosuppressed patients are those produced by cytotoxic agents. The frequency of reactions varies from 100% in AIDS patients with Kaposi's sarcoma receiving in excess of 150 mg of bleomycin[122] to less than 10% in patients receiving most other cytotoxic drugs.[168] The most common pathology is an alveolitis leading to chronic fibrosis, similar to radiation-induced pneumonitis and idiopathic interstitial pneumonitis. The onset can be insidious, and radiographic changes lag behind abnormalities in PFTs.[170] Less commonly, a wide array of noncytotoxic drugs can produce hypersensitivity pathology, including eosinophilic pneumonia, allergic angiitis, and granulomatous reactions.[168,169] A third pattern of pulmonary edema due to a noncardiogenic ARDS reaction has been reported not only with cytotoxic drugs, but also with commonly used drugs such as aspirin and HCTZ.[168,169] Yet another pattern of bronchiolitis obliterans is described with sulfasalazine and penicillamine, but this pattern may be related more to the underlying disease (rheumatoid arthritis) than to the drug.[169] Most of these reactions are associated with a drop in the DLco that precedes radiologic abnormalities or reductions in lung volume. The reactions can occur in three to six weeks or even as acute ARDS, but more commonly occur as the drug effect accumulates in three to six months, as has been best studied with bleomycin.

Most attention has been directed toward bleomycin, since 5% to 10% of patients receiving total doses in excess of 150 mg develop fibrosis[171] and 20% will show a decreased DLco,[170] many without clinical or radiographic changes.[170,172] Cumulative doses greater than 500 mg of either busulfan or bleomycin are associated with sharp increases in pulmonary toxicity.[168] Baseline and serial DLco measurements are imperative to monitor the conditions of patients receiving bleomycin[173]; it is recommended that treatment be stopped if the DLco decreases by more than 35%.[172]

SUMMARY

The primary use of PFTs in immunosuppressed patients is in early diagnosis and as a guide to the prognosis and management of pulmonary complications. Since *P. carinii* pneumonia is the most common and frequently fatal complication, the use of PFTs can largely be defined by that disease. The algorithm presented in Figure 12-5 may be equally applicable to other immunosuppressed patients in whom frequent pulmonary reactions are expected, such as CMV pneumonia, idiopathic interstitial pneumonitis, and graft-vs-host disease in bone marrow transplant patients and bronchiolitis obliterans in heart–lung transplant patients, or interstitial pneumonitis in patients receiving progressive doses of chemotherapy such as bleomycin and busulfan. Emphasis is placed on spirometry because of its ready availability, and on DLco and exercise oxygenation since these have been documented to be the most sensitive of the PFTs.

When an immunosuppressed host is recognized, baseline studies should include a complete blood cell count, chemistry panel, chest radiography, and, in the HIV-positive patient, a T4 cell count. Baseline PFTs including spirometry and DLco are proposed for all immunosuppressed patients, regardless of the results of these studies or the patient's symptomatic state. Baseline resting arterial blood gas measurements are not recommended since they are invasive and not sensitive. Rest and exercise oximetry might be done as a baseline study, but results are unlikely to be abnormal in an immunosuppressed host lacking respiratory symptoms or other evidence of pulmonary disease. Normal values are well established for arterial blood gas measurements and oximetry. Lung volumes and DLco, on the other hand, have a wide range of normality (80% to 120%). The baseline spirometry and DLco are of most value if the patient is free of respiratory illness or is at optimum functional state. Then any future decline will be most sensitively detected.

If baseline spirometry indicates obstructive airways disease, appropriate diagnoses and treatment can be initiated. If the VC is abnormal (<80%

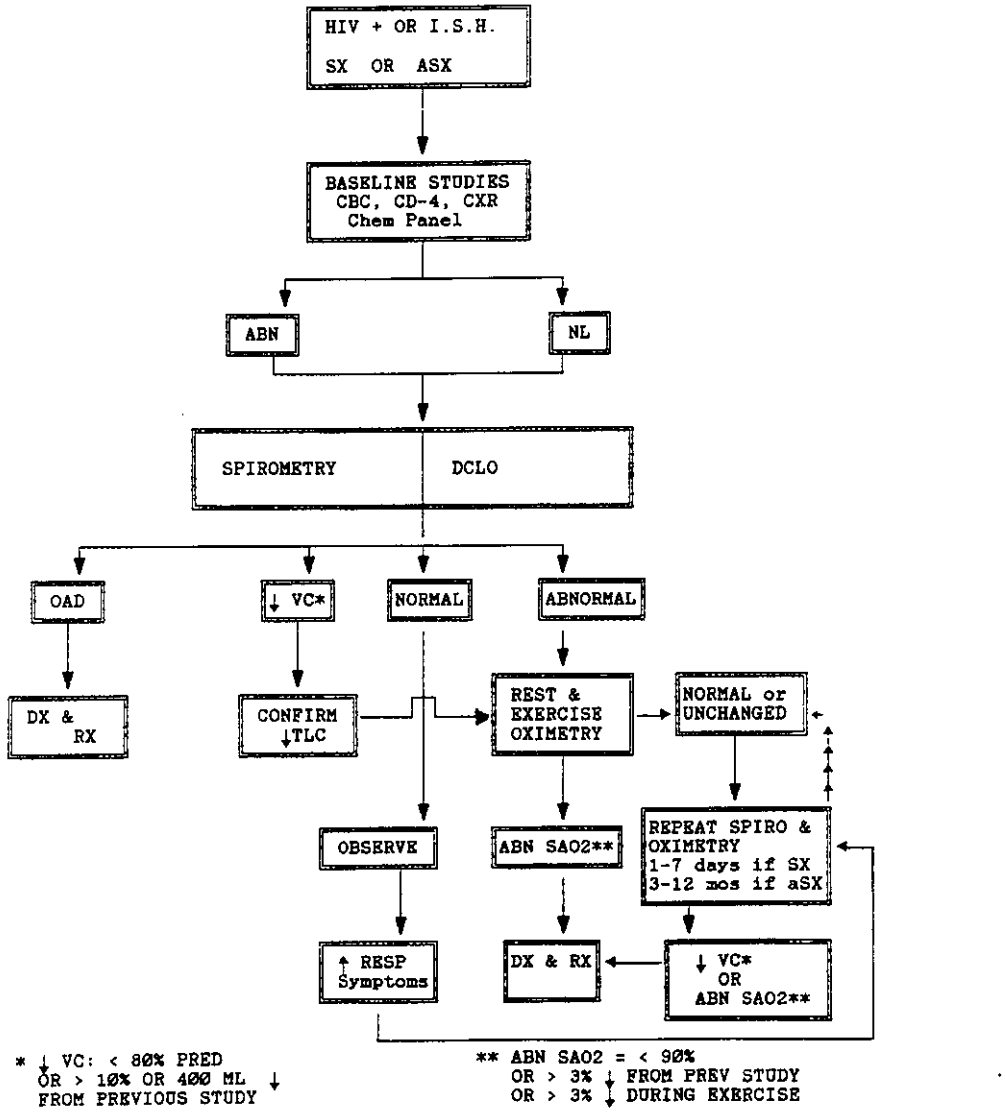

Figure 12-5. Algorithm for workup and monitoring disease progression in immunosuppressed patients, particularly those with AIDS, whether or not symptomatic.

of predicted), with or without obstructive airways disease, then other lung volumes should be measured to confirm and define the degree of restrictive lung disease. If the reduction in lung volume is severe enough (<60% of predicted) or if the DLco is abnormal (<80% of predicted), then rest and exercise oximetry should be performed or arterial blood gas values determined. If oxygenation is abnormal at rest or with exercise (Sao_2 < 90%), additional diagnostic studies and treament are indicated. If the DLco is the only abnormality, as may frequently occur at baseline, particularly in the AIDS population, further studies may be indicated or the patient could be followed by serial studies as indicated by the severity or progressiveness of the symptoms.

When respiratory symptoms occur, office spirometry is a useful initial test, particularly when a baseline study is available for comparison. An increase in or the onset of airway obstruction, and a response to bronchodilators, may explain and treat the respiratory symptoms. A greater than 5% (or 400 mL) decline in VC not explained by airway obstruction or poor patient effort would prompt additional studies, depending on the signs and symptoms.

If the patient's primary complaint is decreased exercise tolerance or dyspnea on exertion, either rest and exercise pulse oximetry or DLco measurements should be done in addition to spirometry and regardless of the results of the spirometry. We favor

pulse oximetry first since it is a noninvasive office procedure. If resting or, more likely, exercise hypoxemia occurs ($Sao_2 < 90\%$), further evaluation is indicated. If the results of oximetry are equivocal (*i.e.*, O_2 saturation 90% to 94%, or <3% decline in Sao_2 from rest or previous baseline measurements) or felt to be inconsistent with clinical assessment, arterial blood gas values and DLco could then be determined to confirm or clarify the oximetry results.

If the results of spirometry, DLco, and oximetry all fail to show any significant changes from baseline, focal or extrapulmonary disease may still be present and additional studies, particularly chest radiography, may also be indicated. The frequency of repeat studies is dictated by the severity of the disease.

The value of spirometry, DLco, and exercise oximetry done at regular intervals in the severely immunosuppressed patient, even without changes in respiratory symptoms, in order to detect disease before symptoms develop is a question currently under prospective study in the AIDS and other immunosuppressed populations.

Glossary

$A-aO_2$	Alveolar-arterial oxygen difference
DLco	Diffusing capacity
Dm	Alveolocapillary membrane
FEV_1	Forced expiratory volume in one second
Fio_2	Fraction of inspired oxygen (%)
FVC	Forced vital capacity
$PA-aO_2$	Partial pressure of alveolar arterial oxygen difference
$PAco_2$	Partial pressure of alveolar carbon dioxide (mmHg)
$Paco_2$	Partial pressure of arterial carbon dioxide (mmHg)
Pao_2	Partial pressure of arterial oxygen (mmHg)
PFT	Pulmonary function tests
RQ	Respiratory quotient
RV	Residual volume
Sao_2	Oxygen saturation
SVC	Slow vital capacity
TLC	Total lung capacity
VA	Alveolar volume
VC	Vital capacity
Vc	Capillary bed
Vco_2	CO2 production
VD	Wasted ventilation
Vo_2	Oxygen consumption

References

1. Permutt S, Chester E, Anderson W et al: Office spirometry in clinical practice: Statement of the American College of Chest Physicians' Committee on Clinic and Office Pulmonary Function Testing. Chest 74(3):298, 1978.
2. Boushey HA, Dawson A: Spirometry and flow-volume curves. In Clausen J (ed): Pulmonary Function Testing: Guidelines and Controversies, Chap 7, p 61. New York, Grune & Stratton, 1982.
3. Dawson A: Spirometry. In Wilson AF (ed): Pulmonary Function Testing: Indications and Interpretations, Chap 2, p 9. New York, Grune & Stratton, 1985.
4. Bates DV, Machlem PT, Christie RV (eds): Respiratory Function in Disease, 2nd ed, pp 10–96. Philadelphia, WB Saunders, 1971.
5. Bates DV (ed): Respiratory Function in Disease, 3rd ed, p 23. Philadelphia, WB Saunders, 1988.
6. Dawson A, Mohler JG: Microprocessor-assisted spirometry. In Clausen J (ed): Pulmonary Function Testing: Guidelines and Controversies, Chap 8, p 83. New York, Grune & Stratton, 1982.
7. Gardner RM, Hankinson JL, Clausen JL et al: Standardization of spirometry—1987 update. Am Rev Respir Dis 136:1285–1298, 1987.
8. Fallat RJ: Bedside pulmonary function and ICU monitoring: Indications and interpretation. In Wilson AF (ed): Pulmonary Function Testing: Indications and Interpretations, Chap 18, p 293. New York, Grune & Stratton, 1985.
9. Ries AL, Clausen JL: Lung volumes. In Wilson AF (ed): Pulmonary Function Testing: Indications and Interpretations, Chap 6, p 69. New York, Grune & Stratton, 1985.
10. Forster RE, Dubois AB, Briscoe WA, Fisher AB (eds): The Lung, 3rd ed, Chap 9, p 223. Chicago, Year Book Medical Publishers, 1986.
11. Burki NK, Albert RK: Noninvasive monitoring of arterial blood gases: A report of the ACCP Section of Respiratory Pathophysiology. Chest 4:666–670, 1983.
12. Neff TA: Routine oximetry: A fifth vital sign? Chest 94(2):227, 1988.
13. Loggan M, Kerby GR, Pingleton SK: Is routine assessment of arterial oxygen saturation in pulmonary outpatients indicated? Chest 94(2):242–244, 1988.
14. Hansen JE, Casaburi R: Validity of ear oximetry in clinical exercise testing. Chest 91(3):333–337, 1987.
15. Van Kessel AL: Pulmonary diffusing capacity for carbon monoxide. In Clausen J (ed): Pulmonary Function Testing: Guidelines and Controversies, Chap 16, p 165. New York, Grune & Stratton, 1982.
16. Ayers LN: Carbon monoxide diffusing capacity. In Wilson AF (ed): Pulmonary Function Testing: Indications and Interpretations, Chap 10, p 137. New York, Grune & Stratton, 1985.
17. Forster RE, Dubois AB, Briscoe WA, Fisher AB (eds): The Lung, 3rd ed, Chap 8, p 190. Chicago, Year Book Medical Publisher, 1986.
18. Crapo JL, Gardner RM, Clausen JL et al: Single breath carbon monoxide diffusing capacity (transfer factor). Am Rev Respir Dis 136:1299–1307, 1987.
19. Sankary RM, Turner J, Lipavsky AJA, Howes EL, Murray JF: Alveolar capillary block in patients with AIDS and *Pneumocystis carinii pneumonia*. Am Rev Respir Dis 137:443–449, 1988.
20. Berven H: Studies on the cardiopulmonary function