Hypoxic pulmonary vasoconstriction (HPV) and vascular remodeling are the most significant dynamic factors. Considerable progress has been made in our understanding of the responses of vascular smooth muscle cells to hypoxia; nevertheless, treatment for cor pulmonale remains largely supportive, directed at improving the hypoxemia with supplemental oxygen and optimizing gas exchange. Pharmacologic attempts directed at pulmonary hypertension have not, to date, shown an impact on long-term function or survival in cor pulmonale.

Recent studies have demonstrated that hypoxic constriction of pulmonary arteries is a unique property of pulmonary artery smooth muscle cells, which appears to be due to hypoxia-induced inhibition of a membrane-bound K⁺ channel, leading to increased intracellular K⁺, membrane depolarization, opening of voltage-gated calcium channels with resultant influx of extracellular Ca²⁺, and vasoconstriction. While the renin-angiotensin system (RAS) is not responsible for this process, which can be induced in isolated vascular rings or single smooth muscle cells, it is certainly possible that RAS activation could promote further vasoconstriction, at least acutely.

In this issue of CHEST (see page 698), Kiely and colleagues report on the effects of the administration of saralasin acetate, a competitive inhibitor of angiotensin II, on acute HPV in normal volunteers. In these subjects, who received diuretics prior to study to activate the RAS, saralasin acetate attenuated the rise in pulmonary artery pressure and vascular resistance produced by breathing hypoxic gas mixtures. Their results suggest that RAS could contribute to the development or maintenance of acute hypoxic pulmonary vasoconstriction. The authors suggest that the newly developed angiotensin II inhibitor drugs, such as losartan potassium, could, therefore, be of therapeutic value in cor pulmonale.

The angiotensin II blocking agents are a new addition to the antihypertensive armamentarium. These drugs work by selectively antagonizing the binding of angiotensin II to the AT₁ receptor, thus inhibiting the vasoconstrictive effects of angiotensin II. Since the angiotensin converting enzyme is not affected, there is no potentiation of bradykinin, as can be seen with the angiotensin converting enzyme inhibitors. In addition to its use in hypertension, preliminary experience suggests that losartan may be useful in treating congestive heart failure, although long-term studies have not been completed.

It is premature, however, to jump on the bandwagon of the treatment of chronic cor pulmonale with yet a new vasodilator agent. First, Kiely and coworkers only studied the effects of saralasin acetate during acute hypoxic ventilation; second, the population selected for study was composed of normal volunteers, not subjects with chronic lung diseases, in whom other factors also contribute to the pulmonary hypertensive state; third, pulmonary hemodynamics were assessed noninvasively, and a number of assumptions were made, including an unchanged downstream (left atrial) pressure after drug administration. The acute and chronic effects of angiotensin inhibition on comprehensively assessed cardiopulmonary hemodynamics, gas exchange, and exercise tolerance in subjects with cor pulmonale should be addressed prior to making any recommendation regarding the potential utility of this approach. Nevertheless, the demonstration by Kiely and colleagues that an angiotensin II blockade may affect HPV in humans opens the door for the exploration of a new and potentially fruitful approach to the prevention and treatment of vasoconstrictive pulmonary vascular disease.

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AIDS-related Non-Hodgkin’s Lymphoma

Useful Techniques for Diagnosis

It has been estimated that among patients infected with HIV, 5 to 10% will have a non-Hodgkin’s lymphoma complicate their course. Patients with HIV are now living longer, attributable to a combination of antiretroviral therapy and improved supportive care.
for infectious complications, so we can only expect the number of cases of AIDS-related non-Hodgkin's lymphoma (NHL) to rise. There are three important differences between NHL found in the HIV population compared with NHL in those who are immunocompetent. First, whether characterized histologically (immunoblastic, large cell, Burkitt's, or diffuse small non-cleaved) or purely in clinical terms, these are rapidly progressing neoplasms, which cause patients' symptoms early in their course and, if untreated, lead to death in weeks to months. Second, AIDS-related NHL is overwhelmingly of B-cell origin, presumably owing to a complex conspiracy of direct effects of the HIV-viral genome (tat protein), Epstein-Barr virus infection, absence of normal immunomodulating function of T-cells, and a variety of autocrine and paracrine growth factor interactions. Third, they involve extranodal sites in most all patients. Although the frequency with which particular extranodal sites are involved varies from series to series, all are agreed that extranodal involvement is the rule rather than the exception. 1-4

The diagnosis of AIDS-related NHL often follows either the development of “B” symptoms, seen in many of the complications of HIV, or when symptoms occur referable to the particular anatomic site of the lymphoma. Knowledge of the techniques to most efficiently discover the diagnosis is critical to the treating physician to intervene expeditiously in the disease process with appropriate therapy, since delays in the diagnosis frequently result in the rapid deterioration of such patients, increasing their probability of treatment-related complications, and compromising their chances for a meaningful remission. Early chemotherapeutic trials in patients with AIDS-related NHL were predicated on the traditional oncology dictum “more is better.” These patients were therefore subjected to intensive chemotherapy designed for the immunocompetent patient, with disastrous results. Unacceptable rates of infectious deaths were common, one series even reporting a 78% incidence of opportunistic infections. Fortunately, as realistic goals of therapy have replaced these inappropriate paradigms, current antineoplastic therapy for these patients uses attenuated dosing schedules with growth factor support. Using such strategies, and stratifying patients according to their HIV helper cell counts and history of opportunistic infections, approximately 50% of patients will achieve a clinical complete remission. The average duration of such remissions is unfortunately only 6 months; however, 20% of patients will have their disease controlled for greater than a year and with acceptable toxicity. 1, 5

When patients with HIV develop pulmonary complaints, the ability to distinguish between infectious, neoplastic, and inflammatory etiologies is obviously critical. In this issue of CHEST (see page 729), Eisner and colleagues report the largest series of patients yet described with pulmonary involvement by AIDS-related NHL. The authors used data obtained from 2 clinical and 2 autopsy-based databases whereby they were able to identify 38 cases of pathologically documented AIDS-related NHL in the chest. Charts of these patients were then reviewed, and clinical, laboratory, radiologic, and diagnostic data were compiled and analyzed. From this, the authors have painted a very useful portrait of pulmonary involvement, which is both interesting and useful to the clinician caring for these patients.

In general, one can conclude that signs and symptoms in these patients are quite nonspecific. Similarly, impaired gas exchange, elevated lactate dehydrogenase, and hematologic abnormalities, all common in AIDS-related NHL, are seen in a great number of other pulmonary complications of HIV. Interestingly, the radiographic features of AIDS-related NHL in the chest are varied, ranging from infiltrates to nodules, effusions, and the frequent finding of lymphadenopathy (54%) in this series. Unfortunately, many of the patients also had coexisting opportunistic infections, and hence it is not clear how frequently the radiographic findings were related to lymphoma or other causes. This point may be seen most clearly from the data regarding diagnostic utility of mediastinoscopy, presumably performed to evaluate adenopathy in the chest and yet diagnostic in only one third of the cases. Recently, Carignan, Staples, and Muller7 reported a series of 18 patients with pathologically demonstrated lymphoproliferative processes in the chest, of which 10 had AIDS-related NHL. They found pulmonary nodules in 90% of patients, either with or without consolidation, and adenopathy in 30%. These findings were also seen in patients with infectious causes and benign lymphoproliferative processes. Therefore, although our awareness of the entity will be enhanced by the current series, there are, in fact, no clinical or radiographic parameters on which to hang one’s hat for the diagnosis.

A firm grasp on the true incidence of clinically meaningful pulmonary lymphoma (ie, complicating the course of a patient being treated who is not in the terminal phase of his/her illness) remains elusive. The authors acknowledge the disparity in their own data between the frequency of involvement in their autopsy series of those with systemic lymphoma (71%) and in their patients obtained solely from the clinical databases (5.8%). They then propose what seems to be a sensible conclusion, namely that pulmonary involvement may be underdiagnosed in the clinical setting, and suggest that it is much more common than previously believed. Furthermore, it may be concluded that
when such patients develop pulmonary complaints, involvement with lymphoma should be strongly considered. One cannot discern, from the data presented in this article, the relative probabilities of a neoplastic vs an infectious explanation in such a setting. Suffice it to say that both are common, and both must be considered.

Certainly the most useful information provided by this article can be found in Figure 1 (see page 732). Here the authors report the yield of various techniques to retrieve diagnostic material from the lungs or pleura. The apparent futility of either bronchoalveolar lavage or bronchial brushings is notable. Although these techniques are useful for documenting infectious etiologies of pulmonary processes in immunocompromised patients, they appear to be of very limited value for the diagnosis of lymphoma. In contrast, however, the results of other commonly employed diagnostic techniques were mixed. The use of transthoracic needle aspiration (TTNA), a commonly used approach in other settings, yielded the diagnosis in only 2 of 9 patients in this series. Whether the now widespread use of flow cytometry to aid our pathologic colleagues will enhance the efficiency TTNA is speculative, but plausible. As mentioned above, mediastinoscopy was diagnostic in only 1 out of 3 patients. The approaches which seemed, from this series, to most frequently produce the diagnosis were transbronchial biopsy (58%), pleural fluid cytology (75%), and open lung biopsy (75%). Viewed from another perspective, however, these data also show the substantial probability of false-negative results from any diagnostic procedure. The clinician can then conclude that in the rare patient where the index of suspicion is high, and knowledge of the diagnosis is critical to the patient’s care, more than one diagnostic test may be required to ultimately make the diagnosis.

In summary, “The pulmonary manifestations of AIDS-related non-Hodgkin’s lymphoma,” despite the problems of a retrospective review, provides treating physicians with a valuable database. It may be concluded that involvement of the lung, pleura, and mediastinal or hilar nodes are more common than previously believed. Finally, until prospective studies are performed and published, the data in this series suggest that the most useful techniques for diagnosis, short of open lung biopsy, are transbronchial biopsy and pleural fluid cytology.

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Pulmonary Function Tests Before Surgery

Surgeons, anesthesiologists, and internists all may care for the patient about to undergo surgery. Assessing the risk of surgery is a necessary part of the presurgical evaluation as the physiologic stress of anesthesia and surgery can be considerable. The carefully rendered medical history and physical examination are the time-honored and proper first steps to evaluate the patient being considered for surgery. Medical leaders through writings, accreditation agencies through the risk of loss of accreditation, and third-party payers through financial reward emphasize the importance of the medical history and physical examination. For many physicians, however, estimates of the level of surgical risk made on the basis of the history and physical are too imprecise: preoperative testing is believed necessary to help refine risk estimates and better guide perioperative management.

Diagnostic testing to help assess surgical risk is seductive to physicians for several reasons. First, test results reported as normal or abnormal based on a cut point seem to offer more certainty than vague medical history or physical examination findings. A cut point in spirometric values below which surgery is believed prohibitive has eluded us to date for most surgery types. Series of patients undergoing major surgery despite very severe spirometric values continue to be published. Second, some patients are reassured by aggressive testing especially when the test process confers little risk itself. The “complete” evaluation by one’s physician suggests great concern for the patient’s welfare and outcome. Third, physicians may receive extra reimbursement for diagnostic testing with some