should be performed in individuals with extrapulmonary TB or 24-55 years of age with pulmonary TB, as well as others with TB at high risk for HIV infection. Every HIV-infected patient with pulmonary symptoms should have a tuberculin skin test (unless known to be tuberculin positive), sputum samples for AFB smear and culture, blood cultures for AFB, stool smear and culture for AFB, and, where appropriate, a bronchoalveolar lavage. If the chest roentgenogram is consistent with tuberculosis (apical infiltrate, cavitary lesion, hilar or mediastinal adenopathy, a miliary pattern, or pleural effusion) every attempt should be made to establish the diagnosis. Pending the outcome of the cultures, and in the absence of an alternative diagnosis adequate to explain the clinical findings, empirical antituberculosis therapy should be considered in this setting; it is mandatory if the patient is tuberculin positive or from a group at high risk of tuberculous infection.

Ventilation must be adequate in areas used to administer inhalation therapy. Health care workers with frequent exposure to HIV-infected individuals should have regular tuberculin skin testing.

If these guidelines are followed, the impact of TB in HIV infection can be lessened.

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Angiotensin-converting Enzyme Inhibitors and Cough

Captopril and the other angiotensin-converting enzyme (ACE) inhibitors are members of a unique class of drugs. Their usage has grown widely during the past decade as preferred treatment for hypertension and congestive heart failure. Although these drugs are dissimilar in several respects, they share important characteristics and a common mechanism of action.

The ACE inhibitors interrupt the renin-angiotensin-aldosterone system through competitive inhibition of angiotensin-converting enzyme. This enzyme, also known as kininase II or bradykinin dehydrogenase, affects two systems simultaneously. It catalyzes both the formation of the direct vasoconstrictor angiotensin II and the breakdown of the autocoid vasodilator bradykinin. Additional effects of angiotensin II include stimulation of aldosterone and suppression of renin secretion. Bradykinin has been shown experimentally to stimulate the production of prostaglandins. Thus, interruption of angiotensin-converting enzyme activity decreases the effects of angiotensin II and increases bradykinin production. These effects translate clinically as a selective lowering of systemic peripheral resistance.

Because the ACE inhibitors enjoy this specificity of action, they are relatively free of adverse effects. In 1988 they gained the status of recommended alternate
first line medications in stepped-care therapy of hypertension. They are currently the drugs of choice for certain groups of hypertensive patients.3

Some side effects cited earlier for captopril have decreased in frequency with modification of dosing schedules. Problems common to the angiotensin-converting enzyme inhibitors as a group are hypotension, which may be addressed by careful attention to hydration and baseline renin levels; renal hemodynamic dysfunction (ACE inhibitors are contraindicated in patients suspected of having bilateral renal artery stenosis or renal artery stenosis in a solitary kidney); angioedema, a rare but life-threatening condition which may be preceded by localized edema; and cough.9

Since first reported as a “nasty dry cough”6 in 1985, captopril-induced cough has become generally acknowledged to be secondary to the ACE inhibitors as a class. It is described as a persistent, vexing, dry cough, sometimes associated with upper respiratory symptoms. ACE inhibitor-induced cough disappears upon discontinuation of the drug. The incidence is variably reported from less than 1 percent to greater than 14 percent, and it is observed more commonly in women than in men.7

The pathogenesis of ACE inhibitor-induced cough has intrigued many investigators since its description. Sesoko and Kaneko,6 in the original case report, speculated that “increased levels of bradykinin and/or prostaglandins” might be involved.

The article by Bucca et al in this issue (see page 1133) offers a coherent and innovative argument for hyperresponsiveness of the extrathoracic airway in these patients. The authors’ introduction provides a fine review of the relationship of bradykinin and the prostaglandins to neural mechanisms and receptors that are linked to cough. The rationale for postulating extrathoracic soft tissue involvement is also well developed. Considering the current broad acceptance of angiotensin-converting enzyme inhibitors, this article is timely. The strength of the authors’ premise rests with validation of the maximal mid-inspiratory flow response to inhaled histamine as an indicator of extrathoracic airway obstruction.

At this time, proven ACE inhibitor-induced cough is an indication to discontinue these medications. Further research is required to justify the treatment of this symptom with additional medications such as prostaglandin inhibitors, or continuation of these drugs at lower dosages, in the presence of cough.

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Hepatopulmonary Syndrome

The term “hepatopulmonary syndrome” can be found in the eighth edition (1989) of Disorders of the Liver and Biliary System by Dame Sheila Sherlock,1 and it was probably first suggested by Eriksson and colleagues6 in Sweden. This syndrome implies a relationship between hypoxemia and pulmonary vascular abnormalities caused by hepatic dysfunction.

Concern regarding the pathophysiology between the liver and the lung has taken on renewed importance in the era of successful liver transplantation.3 Is hypoxemia associated with hepatopulmonary syndrome a contraindication to liver transplantation? How does one recognize the syndrome? Does medical treatment improve hypoxemia? Does hypoxemia resolve following successful transplantation?

As of 1984,4 severe hypoxemia (PaO2 <50 mm Hg) on room air caused by “intrapulmonary shunting” was considered to be an “absolute” contraindication to liver transplantation. With transplantation success over the ensuing years, such hypoxemia is now considered to be a “relative” contraindication to transplantation.5,6

In our opinion, the diagnosis of hepatopulmonary syndrome rests on the following criteria. First, intrapulmonary vascular dilatations must be documented by either contrast-enhanced echocardiography, 99mTc macroaggregated albumin lung scanning, or pulmonary angiography. Contrast-enhanced echocardiography should show delayed echogenicity in the left side of the heart three to six beats following passage of the microbubbles through the right side of the heart; macroaggregated albumin scanning should show up-

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