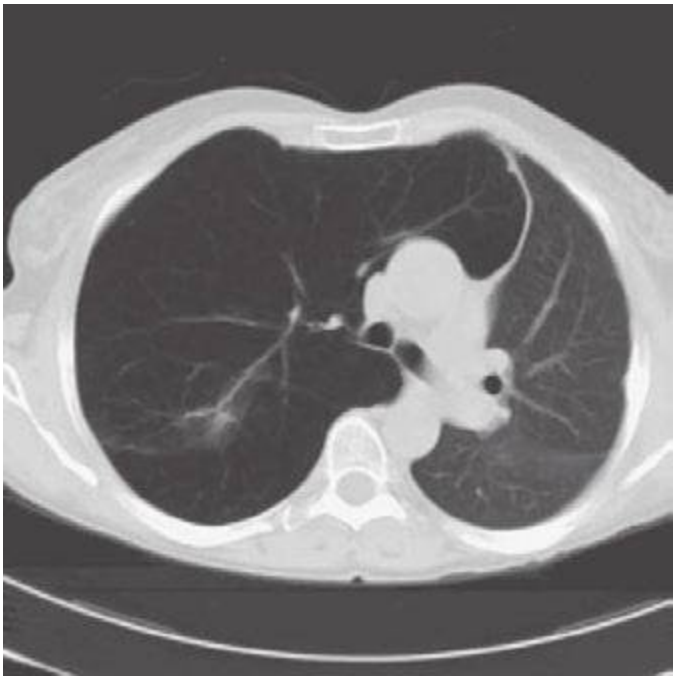

FIGURE 314-4 Chest computed tomography scan of a patient with chronic obstructive pulmonary disease who underwent a left single-lung transplant. Note the reduced parenchymal markings in the right lung (*left side of figure*) as compared to the left lung, representing emphysematous destruction of the lung, and mediastinal shift to the left, indicative of hyperinflation.

about alveolar ventilation and acid-base status by measuring arterial P_{CO_2} and pH. The change in pH with P_{CO_2} is 0.08 units/10 mmHg acutely and 0.03 units/10 mmHg in the chronic state. Knowledge of the arterial pH therefore allows the classification of ventilatory failure, defined as P_{CO_2} >45 mmHg, into acute or chronic conditions. The arterial blood gas is an important component of the evaluation of patients presenting with symptoms of an exacerbation. An elevated hematocrit suggests the presence of chronic hypoxemia, as does the presence of signs of right ventricular hypertrophy.

Radiographic studies may assist in the classification of the type of COPD. Obvious bullae, paucity of parenchymal markings, or hyperlucency suggests the presence of emphysema. Increased lung volumes and flattening of the diaphragm suggest hyperinflation but do not provide information about chronicity of the changes. Computed tomography (CT) scan is the current definitive test for establishing the presence or absence of emphysema in living subjects (Fig. 314-4). From a practical perspective, the CT scan currently does little to influence therapy of COPD except in individuals considering surgical therapy for their disease (described below) and as screening for lung cancer.

Recent guidelines have suggested testing for α_1AT deficiency in all subjects with COPD or asthma with chronic airflow obstruction. Measurement of the serum α_1AT level is a reasonable initial test. For subjects with low α_1AT levels, the definitive diagnosis of α_1AT deficiency requires protease inhibitor (PI) type determination. This is typically performed by isoelectric focusing of serum, which reflects the genotype at the PI locus for the common alleles and many of the rare PI alleles as well. Molecular genotyping of DNA can be performed for the common PI alleles (M, S, and Z).

TREATMENT CHRONIC OBSTRUCTIVE PULMONARY DISEASE

STABLE PHASE COPD

Only three interventions—smoking cessation, oxygen therapy in chronically hypoxemic patients, and lung volume reduction surgery in selected patients with emphysema—have been demonstrated to influence the natural history of patients with COPD. There is currently suggestive, but not definitive, evidence that the use of inhaled glucocorticoids may alter mortality rate (but not lung function). All other current therapies are directed at improving symptoms and decreasing the frequency and severity of exacerbations. The institution of these therapies should involve an assessment of symptoms, potential risks, costs, and benefits of therapy. This should be followed by an assessment of response to therapy, and a decision should be made whether or not to continue treatment.

PHARMACOTHERAPY

Smoking Cessation (See also Chap. 470) It has been shown that middle-aged smokers who were able to successfully stop smoking experienced a significant improvement in the rate of decline in pulmonary function, returning to annual changes similar to that of nonsmoking patients. Thus, all patients with COPD should be strongly urged to quit smoking and educated about the benefits of quitting. An emerging body of evidence demonstrates that combining pharmacotherapy with traditional supportive approaches considerably enhances the chances of successful smoking cessation. There are three principal pharmacologic approaches to the problem: bupropion; nicotine replacement therapy available as gum, transdermal patch, lozenge, inhaler, and nasal spray; and varenicline, a nicotinic acid receptor agonist/antagonist. Current recommendations from the U.S. Surgeon General are that all adult, nonpregnant smokers considering quitting be offered pharmacotherapy, in the absence of any contraindication to treatment.

Bronchodilators In general, bronchodilators are used for symptomatic benefit in patients with COPD. The inhaled route is preferred for medication delivery because the incidence of side effects is lower than that seen with the use of parenteral medication delivery.

Anticholinergic Agents Ipratropium bromide improves symptoms and produces acute improvement in FEV_1. Tiotropium, a long-acting anticholinergic, has been shown to improve symptoms and reduce exacerbations. Studies of both ipratropium and tiotropium have failed to demonstrate that either influences the rate of decline in FEV_1. In a large randomized clinical trial, there was a trend toward reduced mortality rate in the tiotropium-treated patients that approached, but did not reach, statistical significance. Side effects are minor, and a trial of inhaled anticholinergics is recommended in symptomatic patients with COPD. Recent retrospective analyses raised the possibility that anticholinergic use is associated with increased cardiovascular events in the COPD population. This was not demonstrated in a large, prospective randomized trial of tiotropium.

Beta Agonists These provide symptomatic benefit. The main side effects are tremor and tachycardia. Long-acting inhaled β agonists, such as salmeterol or formoterol, have benefits comparable to ipratropium bromide. Their use is more convenient than short-acting agents. The addition of a β agonist to inhaled anticholinergic therapy has been demonstrated to provide incremental benefit. A recent report in asthma suggests that those patients, particularly African Americans, using a long-acting β agonist without concomitant inhaled corticosteroids have an increased risk of deaths from respiratory causes. The applicability of these data to patients with COPD is unclear.

Inhaled Glucocorticoids Although a recent trial demonstrated an apparent benefit from the regular use of inhaled glucocorticoids on the rate of decline of lung function, a number of other well-designed randomized trials have not. Patients studied included those with mild to severe airflow obstruction and current and ex-smokers. Patients with significant acute response to inhaled β agonists were excluded from many of these trials, which may impact the generalizability of the findings. Their use has been associated with increased rates of oropharyngeal candidiasis and an increased rate of loss of bone density. Available data suggest that inhaled glucocorticoids reduce exacerbation frequency by ~25%. The impact of