antiprotease imbalance (involving elastase, αt-antitrypsin and metalloproteinases and their inhibitors) and oxidative stress are also thought to play an important role. Amplifying mechanisms (such as defective antinflammatory responses or latent viral infection) and perpetuating mechanisms are probably important in determining susceptibility to COPD.

In those with emphysema there is enlargement of air spaces and destruction of lung parenchyma. The loss of lung elasticity is associated with closure of small airways and an increase in airways resistance due to reduced radial traction on the airway combined with an increase in dynamic compression during expiration. There is also a reduction in maximum expiratory flow associated with the fall in elastic recoil pressure. The combination of airflow limitation and reduced elastic recoil leads to pulmonary hyperinflation and a fall in lung compliance (see Chapter 3).

The energy cost of breathing is increased in COPD, sometimes to as much as 15% of total body VO2 and ventilatory reserve is reduced; resting ventilation may then constitute as much as 40% of maximum ventilatory capacity.

Although hyperinflation tends to minimize airway obstruction, it adversely affects inspiratory muscle function. The decrease in muscle fibre length reduces the force of contraction, while flattening of the diaphragm, associated with a decrease in its radius of curvature, reduces the efficiency of diaphragmatic pressure generation. Moreover, because of the orientation of the muscle fibres, diaphragmatic contraction may produce ribcage deflation rather than expansion. Similarly, the horizontal position of the ribs makes it more difficult for the respiratory muscles to expand the thorax. In patients with stable COPD, however, it seems that compensatory mechanisms may counterbalance these deleterious effects of hyperinflation on diaphragm function (Levine et al., 1997; Polkey et al., 1995; Rochester, 1991; Similowski et al., 1991).

There is increasing evidence that the inflammatory changes associated with COPD may have deleterious systemic effects contributing, for example, to an increased metabolic rate and weight loss, with skeletal muscle wasting and weakness. Chronic hypoxia and immobility may also contribute to muscle weakness in these patients.

Pulmonary gas exchange is deranged in COPD due to a combination of V/Q mismatch (caused by airways obstruction, pulmonary parenchymal disease and disturbances of the pulmonary vasculature) and hypoventilation. In those with carbon dioxide retention, respiratory drive is usually increased; it is unclear whether a fall in VT contributes to hypercarbia in stable COPD at rest. Those with ARF who develop hypercarbia do, however, breathe at smaller tidal volumes and higher respiratory rates than those who remain eucapnic, probably in an attempt to avoid fatigue and minimize respiratory distress. It seems that, as well as the deterioration in lung mechanics, other factors are likely to contribute to carbon dioxide retention (e.g. hypercarbia can itself have a depressant effect on chemoreceptors). In addition, hypoventilation has the advantage that, as PCO2 rises, a greater volume of carbon dioxide can be excreted for a given level of alveolar ventilation.

In some patients with COPD, alveolar destruction and distortion destroy the capillary bed and, combined with hypoxic pulmonary vasoconstriction, lead to pulmonary hypertension with secondary vascular changes. Cor pulmonale may develop and, during episodes of respiratory failure, worsening hypoxia may precipitate severe right heart failure.

Clinical presentation

ARF complicating COPD is usually precipitated by respiratory tract infection (bacterial or viral) or environmental factors such as air pollution or extremes of temperature. Airways obstruction worsens, with increased production and retention of sputum. Deterioration may also be related to the administration of sedatives or narcotic analgesics, surgery, development of a pneumothorax, rib fractures due to trauma or excessive coughing, pulmonary embolism or congestive heart failure. In some cases, respiratory failure may simply represent the final stages of irreversible lung disease.

Clinically hyperinflation presents as:

- intercostal and supraclavicular recession;
- decreased distance between the cricoid cartilage and the sternal notch;
- reduced cardiac dullness;
- an increased anteroposterior diameter of the chest.

Traditionally two distinct clinical types have been described:

- pink puffers, who present with hyperventilation, severe dyspnoea and relatively normal blood gases; they suffer predominantly from emphysema;
- blue bloaters, whose major abnormality is chronic bronchitis, and who are cyanosed with cor pulmonale, profuse secretions and little or no dyspnoea.

In practice the majority of patients lie somewhere between these two extremes and postmortem studies have not supported this simplistic distinction.

As well as features suggestive of a precipitating infection (fever, purulent sputum, leukocytosis, clinical evidence of pulmonary consolidation, lung infiltrates on chest radiography), patients with acute exacerbations of COPD may present with:

- worsening wheeze;
- dyspnoea;
- tachypnoea;
- use of accessory muscles;
- intercostal and supraclavicular recession;
- pulsus paradoxus;
- ‘pursed-lip’ breathing.
Other features include:

- cyanosis;
- rhonchi;
- prolonged expiration and expiratory wheeze.

Occasionally patients present with increasing hypercarbia and acidosis without dyspnoea (e.g. when their conscious level has been depressed by drugs or in the advanced stages of respiratory failure). Such cases are easily missed. *Cor pulmonale* may be evident as a loud pulmonary component to the second heart sound, a right ventricular heave, jugular venous distension, peripheral oedema and hepatomegaly. *Signs of acute hypercapnia* may also be present, including anxiety, dyspnoea, confusion, transient psychosis, coma and, in some cases, tremors, myoclonic jerks, asterixis and seizures. In addition, cerebral vasodilatation leads to headaches, papilloedema, and occasionally focal neurological signs, while peripheral vasodilatation is associated with warm, flushed skin and a bounding pulse. As $P_{aCO_2}$ rises $P_{aO_2}$ inevitably falls (see Chapter 3) and some believe that many of these features of carbon dioxide narcosis are mediated more by hypoxia and acidosis than by the elevated $PCO_2$.

*Complications* associated with ARF in patients with COPD include pulmonary embolism (which may occur in up to 25% of cases), pneumothorax, gastrointestinal haemorrhage and renal insufficiency. A wide variety of arrhythmias, including premature atrial beats, atrial fibrillation, premature ventricular contractions and ventricular tachycardia, may be encountered.

**Investigations**

A *full blood count* may reveal polycythaemia, which is not only secondary to chronic hypoxia but is also a response to persistently elevated carboxyhaemoglobin levels caused by continued heavy cigarette smoking.

A *chest radiograph* should always be obtained to diagnose or exclude pneumothorax, lobar or segmental collapse, pneumonia or obvious left ventricular failure. The chest radiograph may suggest pulmonary hypertension with prominent proximal and attenuated distal vascular markings, and an enlarged right heart. Radiological features of emphysema include hyperinflation, flattened diaphragms, a vertical heart, vascular attenuation and bullae (Fig. 8.6).

The *ECG* may show features of right atrial and ventricular hypertrophy, including P pulmonale, right-axis deviation, dominant R waves in V1–2, right bundle branch block and ST depression, as well as T-wave flattening and inversion in V1–3.

*Pulmonary function tests* are rarely performed in practice but characteristically show a fall in FEV₁, FVC, and the FEV₁/FVC ratio, a reduced diffusing capacity and an increased residual volume (RV), FRC and TLC. Hypercapnia is unlikely when the FEV₁ exceeds 35% of the predicted value, whilst patients with an FEV₁ of $< 40\%$ of predicted are likely to require hospitalization.

*Sputum* should be sent for microscopy and culture.

**Treatment**

A number of consensus statements and guidelines for the management of acute exacerbations of COPD have been produced (COPD Guidelines Group of the Standards of Care Committee of the BTS, 1997; Pauwels *et al.*, 2001; Table 8.4).

Treatment consists of:

- controlled oxygen therapy;
- elimination of infection with antibiotics (usually a 5–10 day course of doxycycline, amoxicillin, co-amoxiclav, clarithromycin or a quinolone. Moxifloxacin is preferred by some; see Chapter 12);
- bronchodilators and corticosteroids;
- mechanical ventilation when indicated;
- in view of the lack of evidence, chest physiotherapy and mucolytic agents should not be routinely prescribed.

Although acute exacerbations of COPD can be non-infective or due to viral infection, current evidence supports the use of *antibiotics* for acute exacerbations of COPD when sputum is purulent (McCory *et al.*, 2001), particularly in those with severe exacerbations (Stoller, 2002). Although antibiotics are usually recommended for patients with COPD who require mechanical ventilation, there has been little evidence to support this practice in those without pneumonia. However, a prospective, randomized, controlled trial has demonstrated that, when compared to placebo, once-daily oral ofloxacin significantly reduced mortality, duration of ventilation and