The management of severe chronic obstructive pulmonary disease

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Chronic obstructive pulmonary disease (COPD) is common and often not identified until the patient is admitted with an acute exacerbation. By this time, FEV1 is usually less than 40% predicted and there is significant exercise limitation and impairment of quality of life. Recent data have allowed rational treatment to be planned even in advanced disease. Management falls under three headings:

- patient assessment
- staged delivery of outpatient care
- treatment of the acute exacerbation.

Patient assessment

Clinical

Strong pointers to COPD in the history are:

- persistent exertional dyspnoea developing over a number of years, plus or minus cough and sputum production
- a smoking history of more than 20 pack-years
- general practitioner attendances for antibiotics in the winter.

Physical findings may be absent or involve changes in chest wall configuration (overinflation, prominent abdomen, indrawing of the lower ribs) or breathing pattern (use of accessory muscles, pursed lip breathing). Cyanosis may be present, but is difficult to detect. Elevation of the jugular venous pulse and peripheral oedema suggest fluid retention which may be secondary to lung disease. This is likely only if the PaO2 is greater than 7.3 kPa.

Physiological

Reduction in the FEV1, which does not improve substantially either spontaneously or in response to treatment is the hallmark of COPD. Failure to measure this is equivalent to omitting the blood pressure in assessing hypertension.

The FEV1, is reproducible and simple to perform. A change of less than 200 ml may arise by chance. Provided that the patient has evidence of airflow obstruction (i.e. FEV1/FVC <70%) disease severity can be expressed in terms of the FEV1, percentage predicted. Patients with an FEV1, less than 60% predicted have moderate disease, and those less than 40% severe disease. FEV1, is a prognostic index, but a poor descriptor of the impact of the illness on the patient — a good history is also needed.

Changes in static lung volumes parallel the changes in FEV1. Carbon monoxide transfer factor (D,CO) is a reasonable surrogate for the presence of emphysema except in the most severe cases where it is difficult to measure. A normal D,CO is compatible with COPD but a high value suggests the possibility of bronchial asthma.

Bronchodilator reversibility testing

Bronchodilator reversibility testing is valuable in excluding asthma and in establishing a baseline of best performance, but it does not predict the response to therapy. There is no generally agreed protocol. One approach is to measure FEV1, before and 45 minutes after a combination of nebulised salbutamol (5 mg) and ipratropium (500 μg). Combinations of bronchodilator drugs are more likely to detect responders (Fig 1). A change of 15% from baseline which exceeds 200 ml (the approximate reproducibility of the FEV1,) is unlikely to arise by chance.

Most COPD patients show a small improvement in FEV1 of 200-400 ml if the testing is repeated often enough. Larger changes are infrequent and suggest a more ‘asthmatic’ illness.

Oral corticosteroid trials

Trials of oral corticosteroids can identify ‘corticosteroid-responsive COPD’. However, recent data suggest that some benefit can occur with inhaled corticosteroids in patients with a ‘negative’ corticosteroid trial. FEV1, is measured before and two weeks after 30 mg/day of oral prednisolone. A significant change is defined as an increase in FEV1, of 150 ml.

Management of stable disease

Key elements to the treatment approach to COPD and the stages at which they can usefully be introduced are shown in Fig 2. Treatment is cumulative, and some elements such as smoking cessation form part of treatment at all stages of the illness.
Smoking cessation

Stopping smoking is worthwhile even in advanced disease. The use of nicotine replacement therapy and access to patient support groups significantly increase the quit rate.

Bronchodilator therapy

All bronchodilators improve breathlessness and exercise performance in stable COPD irrespective of the changes in FEV₁. Inhaled drugs have fewer side effects, are better tolerated and suitable for acute symptom relief. Unlike bronchial asthma, beta-agonists and anticholinergics are equally effective. In this older population, tremor and palpitations are troublesome with beta-agonists, whilst dry mouth and a bitter taste are common with anticholinergics. Either can be used as rescue treatment.

Maintenance treatment is feasible with either class of drug alone or preferably in combination. Regular treatment (at least four times daily) is needed to obtain maximum effect. Long-acting inhaled beta-agonists such as salmeterol are well tolerated and improve quality of life. Nebulised bronchodilator treatment is poorly studied and prescription complicated by a placebo effect. Patients treated at home who show a 10% increase in mean peak flow over two weeks may be those best suited to this therapy. Oral theophyllines improve exercise tolerance and quality of life in the limited number of patients able to tolerate the high doses needed to produce these effects.

Inhaled corticosteroids

Inhaled corticosteroids are indicated when there is a clear (ie >400 ml) response after an oral corticosteroid trial. They do not modify the rate of decline of FEV₁, but reduce the number of exacerbations of disease and limit the decline in health status even in patients who are corticosteroid trial-negative. Benefits in patients with no history of previous exacerbations are very limited. Skin bruising can occur.

Table 1. Practical aspects of pulmonary rehabilitation.

| Assessment: | Physiological | Spirometry before and after bronchodilator (lung volumes, respiratory pressures, PI and Pemax) |
|-------------|---------------|-----------------------------------------------------------------------------------------------|
| Functional  | 6-min or shuttle walk test, intensity of dyspnoea during exercise |
| Global      | MRC dyspnoea scale, Hospital Anxiety and Depression questionnaire (health status questionnaires eg St George's, Chronic Respiratory Disease, SF-36) |
| Patient education | About: the nature of COPD, when and how to use their treatment = inhaler technique, the purpose of the rehabilitation programme = SMOKING CESSATION |
| Intervention: | Optimise existing treatment |
| Exercise    | The most important component; whole body symptom-limited and built up to 20 min continuous exercise per day; individual targets: specific respiratory muscle training may help some patients |
| Oxygen      | Consider need for domiciliary oxygen on basis of blood gas tensions; portable oxygen may improve exercise capacity, but not widely available in the UK |
| Nutrition   | Identify specific problems eg bloating after food (take smaller, more frequent meals); increase carbohydrate intake, especially if patient is thin and takes regular exercise |
| Delivery of care | Outpatient classes 2–3 times weekly, 6–8 weeks per course, 6–8 participants per class |
| Barriers to uptake | Social isolation, significant comorbidity, depression, continued heavy smoking |

Options in brackets indicate validated measures used in research-based programmes.

COPD = chronic obstructive pulmonary disease; MRC = Medical Research Council. PI = maximum respiratory pressure Pemax = maximum expiratory pressure
Key Points

► An objective diagnosis based on spirometry is needed if COPD management is to be effective.
► The response to bronchodilator therapy is best judged by the improvement in the patient’s symptoms and exercise performance rather than by the change in FEV₁, which is often quite small.
► Inhaled corticosteroids are only indicated in patients with a relatively large bronchodilator response and in those with a history of exacerbations requiring oral corticosteroid therapy.
► Pulmonary rehabilitation can have a substantial effect on exercise capacity and health status but is most effective in ambulatory patients who are not housebound.
► Acute exacerbations of COPD can be managed at home safely with a hospital-to-home team provided there is no major co-morbidity and the arterial pH is normal.

Pulmonary rehabilitation

Despite the evidence that pulmonary rehabilitation helps patients with stable COPD, it is not yet widely used in the UK. Key aspects of the programme are given in Table 1. Outpatients attend a group 2–3 times weekly, with 6–8 in each class. Treatment benefits can last for six or more months. Patient selection is important, and many patients with severe COPD presenting to hospital (FEV₁ <30% predicted) are too disabled to improve. Social isolation, limited access to transport and poor motivation are predictors of a poor outcome.

Oxygen treatment

Patients with persistent hypoxaemia (PaO₂ <7.3 kPa breathing air) when clinically stable have improved survival if they can increase their PaO₂ to >8.0 kPa for 15+ hours per day (Fig 3)⁷⁻⁹. Despite this clear evidence, oxygen treatment is still misused. Common problems are:

- failure to assess when patients are clinically stable
- failure to measure PaO₂ before treatment
- poor patient compliance.

Prescribing oxygen to patients with a PaO₂ >7.3 kPa is not beneficial. Administration of oxygen during exercise improves exercise tolerance. Symptomatic therapy with home cylinder oxygen is commonly prescribed, but evidence of benefit is lacking.

Nutrition

A low body mass index (<23 kg/m²) is an independent predictor of mortality in advanced COPD (Fig 4)⁸. Muscle wasting is associated with reduced exercise capacity and peripheral myopathy. No specific treatment reverses these changes, but increased calorie intake and exercise may be beneficial.

Surgical therapy

The removal of large ‘space-occupying’ bullae can produce dramatic symptomo-
matic improvements in selected COPD patients. This approach has recently been extended to remove areas of macroscopic emphysema identified by computed tomography scan. This increases FEV₁ and six-minute walking distance, and improves quality of life⁹. Patient selection is crucial (Table 2). Long-term follow-up data are limited, and the US National Emphysema Treatment Trial should clarify the role of this type of surgery. Lung transplantation is of only palliative value in COPD, its success being limited by the availability of organ donors, the development of obliterative bronchiolitis and systemic side effects of immunosuppressive drugs.

**Treatment of acute exacerbations**

Acute exacerbations of COPD are characterised by an increase in symptom intensity associated with an increase in sputum volume and purulence. PaO₂ is usually reduced and carbon dioxide (CO₂) retention may occur, causing a fall in pH. Exacerbations with a normal pH (>7.32) are seldom fatal. Medical management, which is relatively stereotyped but influenced by the blood gas tensions, comprises the following:

- **Controlled oxygen therapy** aims for a SaO₂ of over 90%. This is a threshold value and there is no dose-response relationship. An SaO₂ of 98% that causes CO₂ retention is unnecessary and dangerous. The accuracy of Venturi mask treatment should be set against the greater chance that nasal prongs will remain in contact with the patient.

- **Nebulised bronchodilators** reduce dyspnoea and can be given up to six times a day without excessive side effects. There is no evidence that either beta-agonists or anticholinergics are superior, nor is combination therapy of clear benefit. The usual doses are 5 mg of nebulised salbutamol and 500 µg of ipratropium.

- **Intravenous theophylline infusion**. There is no objective evidence that intravenous theophylline infusion is valuable either on its own or in addition to nebulised bronchodilators.

- **Oral corticosteroids** increase the rate of resolution of exacerbation in hospitalised patients with COPD, shorten their hospital stay and are well tolerated (Fig 5)¹¹.¹². There is no advantage in prolonged courses, intravenous administration or very high doses: 30 mg of prednisolone as a single dose for 7–10 days is usually adequate.

- **Antibiotic therapy** is indicated when there is evidence of systemic upset (eg fever, raised white blood cell count) and/or increased sputum volume and purulence, but is of no

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**Table 2. Selection criteria for lung volume reduction surgery.**

| Inclusion                       | Exclusion                                |
|---------------------------------|------------------------------------------|
| FEV₁ <25% predicted            | significant hypercapnia                  |
| elevated functional residual capacity; high RV/TLC ratio | significant comorbidity, especially ischaemic heart disease |
| low flat hemidiaphragms         | alpha-1-anti-trypsin deficiency           |
| heterogeneous distribution of emphysema on CT with upper lobe predominance | significant bronchiectasis - some minor abnormalities evident on CT, including small pulmonary nodules and bullae, can be dealt with at operation |
| ability to complete inpatient pulmonary rehabilitation programme |

CT = computed tomography; RV = residual volume; TLC = total lung capacity
value in their absence. Oral therapy is as effective and better tolerated than intravenous treatment. The major pathogens are *Streptococcus pneumoniae* and *Haemophilus influenzae*, although epidemics of *Moraxella catarrhalis* can occur and are resistant to conventional treatment with amoxycillin or erythromycin.

- **Respiratory stimulants.** Patients developing hypercapnia and acidosis are candidates for ventilatory support. Some patients can be managed by infusion of doxapram hydrochloride, a non-specific but relatively safe ventilatory stimulant. This may be inferior to non-invasive positive pressure ventilation when used alone, but can be useful when other resources are unavailable.

### Home care

The large numbers of patients hospitalised with exacerbations of COPD, and the relatively benign course of those with a normal pH, have led to the concept of 'hospital at home' care for selected patients. Assessment in the accident and emergency department is necessary if this is to be effective. Patients with a normal chest X-ray and a pH of >7.32 can be successfully supported at home using nebulised bronchodilators, corticosteroids, antibiotics and an oxygen concentrator if indicated\(^1\). These services are led by nurse practitioners who undertake home visits until recovery has occurred. The readmission rate appears acceptable, but no randomised control trials have been reported.

### References

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Non-invasive positive pressure ventilation

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In the late 1980s non-invasive positive pressure ventilation (NPPV) was developed for the domiciliary management of chronic hypercapnic ventilatory failure, in preference to negative pressure ventilation. As confidence in the technique grew, patients with acute-on-chronic ventilatory failure were ventilated in hospital. This article reviews the uses of NPPV in both chronic and acute respiratory failure (RF).

Chronic respiratory failure due to neuromuscular disease or chest wall deformity

In general, hypercapnic RF worsens during sleep because of a normal physiological drop in respiratory drive. Initially, patients develop RF only at night, managing to maintain a normal carbon dioxide tension during the day. At this stage, an otherwise unexplained rise in base excess in the blood may be a clue to the presence of nocturnal hyperventilation. As the disease progresses, however, abnormal blood gas tensions develop during the day. Symptoms are non-specific and may be mistaken for a 'normal' part of the underlying disease; they include lethargy, sleepiness, morning headache, neuropsychiatric symptoms, dyspnoea and ankle oedema (which may be mistaken for heart failure). In addition, these patients are at risk of sudden life-threatening deterioration, for example with a trivial chest infection. Unfortunately, patients with chest wall deformity (CWD) or neuromuscular disease (NMD) not infrequently present as an emergency, sometimes requiring intubation and mechanical ventilation, with a history typical of nocturnal hyperventilation going back over many months. Because symptoms are so non-specific, it is important to have a high index of suspicion in 'at risk' individuals (Table 1) and a low threshold for further investigation.

Investigation

Patients at risk of developing nocturnal hyperventilation should be assessed at an early stage by a respiratory physician, since the need for assisted ventilation can often be anticipated by observing trends in physiological measurements. Patients should be warned of the symptoms of nocturnal hyperventilation, and those with a weak cough can be taught how to maximise secretion clearance.

Table 1. Causes of chronic type II respiratory failure22

| Condition                      | Notes |
|-------------------------------|-------|
| Central hypoventilation syndrome |      |
| Ondine's curse                 |       |
| Spinal cord injury - tetraplegia |   |
| Poliomyelitis                  |       |
| Diaphragmatic paralysis        |       |
| Metabolic myopathies           |       |
| Spinal muscular atrophy        |       |
| Congenital myopathies          |       |

Progressive neuromuscular disorders:
- Duchenne muscular dystrophy
- Amyotrophic lateral sclerosis (motor neuron disease)

Obstructive lung disease:
- chronic obstructive pulmonary disease
- bronchiectasis, cystic fibrosis