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Chronic Obstructive Pulmonary Disease

Abstract

Chronic obstructive pulmonary disease is a widely prevalent condition usually associated with cigarette consumption. It has a worldwide impact on the allocation of health care resources. The diagnosis is made by history and physical examination supported by measures of airflow and lung volume. The levels of impairment, disability and handicap dictate the requirements for medical care. Smoking cessation, immunization, maximal pharmacologic therapy including the use of supplemental oxygen and prompt attention to exacerbations, represent the basic principles of management. Pulmonary rehabilitation has been shown in a number of randomized clinical trials to improve functional exercise capacity and health-related quality of life. Many interesting approaches, such as lung volume reduction, lung transplantation, nutritional support and mechanical ventilation for acute exacerbations, are in various stages of clinical use and evaluation.

Introduction

Chronic obstructive pulmonary disease (COPD) is a broad topic supported by an extensive research and clinical literature. In

the following overview I would like to identify some of the key clinical points including aetiological factors, pathophysiology and current management approaches that are likely to be of help to those who encounter patients

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with COPD in their clinical practice. For additional material the reader is referred to two excellent recent overviews of 'Standards for the Diagnosis and Care of Patients with Chronic Obstructive Pulmonary Disease' [1] and 'COPD: Current Concepts and Future Prospects' [2].

COPD has been estimated to affect 5% of the world's population. It is a leading cause of death that continues to increase in prevalence. Those who have it require ongoing health care. They are also removed from the work force on intermittent basis. Over the last 10 years prevalence rates for men have changed only slightly whereas those for women have increased dramatically [3, 4]. The notion that therapy is pointless, since airway obstruction is fixed, is incorrect and neglects the many advances in our understanding of the pathophysiology and management of this condition. In fact COPD is a fascinating condition embodying challenges across the spectrum of medicine from public health (smoking prevention and cessation) to the latest in surgical (lung volume reduction, lung transplantation) and molecular biological (detailed pathophysiology, susceptibility to nicotine and genetic replacement of enzyme deficiencies) techniques. Moreover it is a condition in which both physicians and non-physician health care professionals will impact on the health care of a large numbers of individuals.

Pathophysiology of COPD

Chronic bronchitis is characterized initially by a productive winter cough that may progress to persist throughout the year [5]. Patients with bronchitis develop airway inflammation of the respiratory and membranous bronchioles. Such inflammation is associated with mucous hypersecretion, inflammatory narrowing and obstruction to airflow. Many

patients with only bronchitis have a persistent productive cough and do not develop substantial dyspnoea or functional exercise limitation. In fact excellent epidemiological studies have suggested that chronic bronchitis alone is unlikely to be associated with substantial symptoms outside of a productive cough and infectious respiratory exacerbations. Emphysema by contrast is defined (pathologically rather than clinically) by the destruction of air spaces beyond the terminal bronchioles resulting in their enlargement and lack of uniformity.

Both conditions often exist together and account for the resulting changes in impairment (change in anatomical structure or physiological function), disability (reduction in ability to perform certain functions such as walking or stair climbing) and handicap (the societal equation when impairment and disability are imposed on life-style) associated with COPD. Airflow limitation occurs from the destructive (emphysematous) loss of elastic recoil, small airway mucous hypersecretion, inflammatory cell infiltration, fibrosis and smooth muscle hypertrophy (bronchitis). There are measurable reductions in the forced expired volume in 1 s (FEV_1 , fig. 1) as well as other spirometric measures of impairment (maximal flow at 50% and 25% vital capacity, FEV_1/FVC , etc.) [6–9]. Loss of elastic recoil also results in an increased residual volume, functional residual capacity and total lung capacity. As the patient seeks to reduce the work of breathing by breathing at a higher lung volume there is clinical (barrel chest, tracheal tug, indrawn intercostal muscles, prominent accessory muscles) as well as radiological evidence of hyperinflation. Damage to the alveolar/capillary interface reduces the surface of the lung available for gas exchange and alters the ventilation-perfusion relationships within the respiratory units. The two extremes of mismatching, namely dead-space

Fig. 1. The relationship between FEV₁, age and smoking. In non-smokers or those who are not susceptible to smoke the FEV₁ falls at approximately 25 ml/year. Smokers who are susceptible decline at a faster rate which may reach as high as 75–80 ml/year. The rate of decline in FEV₁ for those who discontinue smoking approaches that of a non-smoker. This is a simplified model that relates the decline in FEV₁ to age and smoking history. There is an appreciable between-individual variation. Undoubtedly other factors such as genetic susceptibility modify the process [9].

ventilation (with little or no perfusion) and shunt (perfusion with little or no ventilation) influence the work of breathing as well as the ability of the lung to adequately oxygenate the blood. In advanced stages of the disease alveolar hypoventilation results in hypercapnia (ventilatory failure).

Although asthma is characterized by airway obstruction that may become chronic, the differences in pathophysiology, target population and approaches to management between asthma, bronchitis and emphysema are such that it is helpful to consider asthma as a separate entity. Notwithstanding the above, in some individuals COPD is associated with both variability and reversibility of airflows reflecting an overlap between COPD and asthma that offers additional management opportunities.

Clinical Features

Patients with COPD usually have a history of smoking a package of cigarettes per day for several years. Their presenting complaint is often of a productive cough or an acute respiratory tract infection. The cough is initially confined to the morning, the sputum being mucoid and becoming purulent during exacerbations. Wheezing is often noted during respiratory tract infections. With time (and further smoking) the intervals between infectious exacerbations shorten and a permanent productive cough as well as frequent wheezing may be identified. Alternatively, dyspnoea on exertion becomes the predominant clinical complaint with a decreasing exercise tolerance which progresses to limit self-care activities such as washing, dressing and eating. Although the primary impairment is respiratory, an individual with COPD is likely to have secondary impairments which include poor general fitness (deconditioning) as well

as the psychosocial sequelae of anxiety, depression and fear.

The findings on examination depend on the extent of the COPD. Wheezing on forced expiration may be one of the earliest signs. Patients who are hyperinflated will have an increase in the anteroposterior diameter of their chest and a low diaphragm which moves poorly during respiration. The chest is resonant to percussion and breath sounds are distant as are the cardiac sounds. As the condition progresses patients adopt postures to ease their sense of dyspnoea, leaning forward on their elbows or palms and breathing through pursed lips with the assistance of their accessory muscles of respiration. Those who develop hypoxia and right heart failure (blue bloaters) appear different from those who remain pink, skinny and profoundly dyspnoeic (pink puffers). The reasons as to why a particular clinical constellation predominates have been the subject of considerable discussion and involve mechanisms of respiratory control as well as the more local distribution of the lung disease.

Relevant diagnostic support comes from spirometric measures that reflect an irreversible or only slightly reversible reduction of airflow. More sophisticated measures of diffusion, total lung capacity and gas trapping are interesting and useful in specific circumstances but not generally essential for good clinical practice. Radiologic measures that reflect hyperinflation such as an increase in the anteroposterior diameter of the chest radiograph, flattening of the diaphragms and an increase in the retrosternal airspace, provide useful confirmatory evidence. Enlargement of the pulmonary arteries and an increase in the right heart size may reflect pulmonary hypertension. High resolution CT scanning is more sensitive than chest radiography and reflects the anatomical distribution of the emphysema. Such investigations are helpful if surgery is being considered.

Management

It is important to approach the management of patients with COPD with an understanding that the condition varies among patients and that it may vary considerably, with time, for any individual patient. Patients with mild airflow obstruction ($FEV_1 > 50\%$ predicted) [8–12] have fewer requirements as their level of disability is mild. They should of course discontinue smoking and may require bronchodilators on an as needed basis, for example in relationship to exercise or an infectious respiratory exacerbation. At the other end of the spectrum are those with severe COPD ($FEV_1 < 35\%$ predicted). Although they comprise the minority of patients, they have a profound impact on the allocation of health care resources. They frequently require ongoing specialist supervision and a variety of medications, including oxygen. They are prone to frequent respiratory exacerbations, often associated with increasing disability and handicap. A multidisciplinary approach is preferable to a purely physician-centered approach as non-physician professionals (respiratory, physical and occupational therapy, social work, nursing, dietary counseling, etc.) will often be able to address patient and family issues more effectively than the physician alone. An overall scheme of managing those with COPD is summarized in figure 2. General principles of management include fostering healthy lifestyle habits, avoidance of situations likely to precipitate exacerbations, appropriate influenza (and sometimes pneumococcal) vaccination, good diet, regular exercise etc.

Those individuals in whom the impairment is moderate ($FEV_1 49\text{--}35\%$) fall within the above spectrum, sometimes requiring intense specialist management and at other times being readily managed by their primary care physician. Whatever their level of impairment an ongoing dialogue will promote

Fig. 2. Summary of an algorithmic approach to the management of individuals with COPD. It forms a framework beginning with establishing the diagnosis and assessing the symptoms and addressing the necessary key steps including cessation of smoking, maximizing the use of bronchodilators, assessing for supplemental oxygen and referring to a multidisciplinary rehabilitation programme [1].

patient education and hopefully compliance with the principles of management [10–12]. Prompt attention to infectious exacerbations is also important. Patients can be taught to recognize and promptly respond to changes in their condition.

Smoking Cessation

When considering the risk factors for developing COPD, active cigarette smoking is by far the most important [13–15]. Other risks such as environmental pollution, passive smoking and genetic predispositions such as α_1 -antitrypsin deficiency are of very little importance in the majority of cases (table 1).

Table 1. Risk factors for COPD

Cigarette smoke
Other environmental and behavioural factors
Air pollution
Occupational exposures to particulate dusts
Intravenous drug abuse or talcosis
Treatable constitutional and genetic factors
Low body mass index
Protease inhibitor deficiency or phenotype
Bronchial hyperreactivity
Untreatable demographic and genetic factors
Age
Family history of COPD
Male sex

From Fagerstrom and Schneider [14].

The FEV₁ declines by 25–30 ml per year in non-smokers and at an accelerated rate in susceptible smokers sometimes reaching a decline of 150 ml per year. Those who discontinue smoking influence the rate of decline of their FEV₁, which soon approaches that of non-smokers.

Physicians and non-physician health care professionals can play an essential role in promoting a good understanding of the dangers of smoking among the actively smoking population and among those especially at risk (adolescents). The 5 stages of quitting smoking include: pre-contemplation, contemplation, preparation, action and maintenance. Ways in which the smoker may be helped include setting a quit date, ensuring support from family and friends, referral to smoking cessation groups and actively encouraging maintenance of smoking cessation. It is also important to identify underlying factors such as depression, stressful home or working environments and conditioned addictive behaviours that may retard efforts to discontinue smoking. Nicotine replacement is available both in chewing gum and by transdermal

Table 2. Protocol for smoking cessation

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1	Initiation
Physician or health care worker should initiate quitting, explaining risks of cigarette smoking for the individual and including strong admonition. Encourage establishment of a definite quit date. Offer referral for self-help or group programme.
2	Early follow-up
Telephone patient on or within 3–5 days after quit date. Review progress and counsel regarding recruitment of support person. Call again 1–2 weeks after quit date. Repeat as needed.
3	Continuing reinforcement
Further follow-up should be arranged by physician or health care worker. Next regular visit should be less than 2 months after initiating cessation programme: assess progress with CO and expired air and/or cotinine in urine, blood or saliva. If abstinent, review and reward success and reinforce prior warnings. May follow by phone monthly until next visit; continue follow-up at increasing intervals for 12 months after quit date.
4	Failure or recidivism
If patient fails to achieve abstinence or does so but relapses, physician or health care worker should review the programme with patient, emphasizing elements of success and identifying circumstances of failure; explore alternatives. Nicotine replacement may be offered to control withdrawal symptoms; infrequently, other pharmacologic therapy such as clonidine or bupropion may be discussed. Hypnosis may be considered but is of little value when as a single-session recourse. Acupuncture is not recommended.
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From Fiore et al. [15].

patch. For some individuals who experience very unpleasant withdrawal effects (anxiety, irritability, difficulty concentrating) replacement with non-cigarette nicotine may enhance the possibility of sustained smoking cessation (table 2).

Immunization

Both influenza and pneumococcal vaccine are recommended to prevent the infectious complications that involve the respiratory tract. In fact the evidence that they do so remains equivocal [16–18].

Pharmacologic Therapy

Table 3 summarizes a step-by-step approach to the pharmacological management of those with COPD. The table indicates management for those with mild or moderate disease as well as the options for those in whom control is suboptimal and those undergoing severe exacerbations.

Sympathomimetics

β_2 -Agonists frequently provide symptomatic relief even if spirometry does not change. If symptoms are intermittent then a selective β_2 -agonist administered by metered dose inhalation is a reasonable approach. Table 4 summarizes the characteristics of several available bronchodilators that may be delivered by metered dose inhalers. Such tables present a useful summary but invariably require updating as new products enter the market. Delivery may be enhanced with a spacing device although a variety of other approaches (diskhalers, spinhalers, etc.) have become available. Side-effects of the more selective β_2 -agonists are less than the non-selective medications such as ephedrine, isoproterenol and epinephrine. Nevertheless they include tremor, nervousness and palpitations especially in the elderly. β_2 -Agonists are often administered 4–5 times per day but there is no evidence to support their regular rather than their symptomatic use [19–21]. Newer

Table 3. Step-by-step pharmacologic therapy for COPD

- 1 For mild, variable symptoms:
 - Selective β_2 -agonist metered dose inhaler (MDI) aerosol, 1–2 puffs every 2–6 h as needed or not to exceed 8–12 puffs per 24 h
- 2 For mild to moderate continuing symptoms:
 - Ipratropium MDI aerosol, 2–6 puffs every 6–8 h; not to be used more frequently
 - plus
 - Selective β_2 -agonist MDI aerosol, 1–4 puffs as required 4 times daily for rapid relief, when needed or as regular supplement
- 3 If response to step 2 is unsatisfactory, or there is a mild to moderate increase in symptoms:
 - Add sustained release theophylline, 200–400 mg twice daily or 400–800 mg at bedtime for nocturnal bronchospasm
 - and/or
 - Consider use of sustained release albuterol, 4–8 mg twice daily or at night only
 - and/or
 - Consider use of mucokinetic agent
- 4 If control of symptoms is suboptimal:
 - Consider course of oral steroids (e.g. prednisone), up to 40 mg/day for 10–14 days
 - If improvement occurs, wean to low daily or alternate day dose, e.g. 7.5 mg
 - If no improvement occurs, stop abruptly
 - If steroid appears to help, consider possible use of aerosol MDI, particularly if patient has evidence of bronchial hyperreactivity
- 5 For severe exacerbation
 - Increase β_2 -agonist dosage, e.g. MDI with spacer 6–8 puffs every 0.5–2 h or inhalation solution, unit dose every 0.5–2 h or subcutaneous administration of epinephrine or terbutaline, 0.1–0.5 ml
 - and/or
 - Increase ipratropium dosage, e.g. MDI with spacer 6–8 puffs every 3–4 h or inhalant solution of ipratropium 0.5 mg every 4–8 h
 - and
 - Provide theophylline dosage intravenously with calculated amount to bring serum level to 10–12 g/ml
 - and
 - Provide methylprednisolone dosage intravenously giving 50–100 mg immediately, then every 6–8 h; taper as soon as possible
 - and add:
 - An antibiotic, if indicated
 - A mucokinetic agent if sputum is very viscous

From Fiore et al. [15].

Table 4. Characteristics of bronchodilators delivered by metered dose inhalers

Medication	Dose/puff mg	Level of activity ¹			Time of effect, min		
		β_1 -agonist	β_2 -agonist	anticholinergic	onset	peak	duration
Isoproterenol	0.08	+++	+++	–	3– 5	5– 10	60– 90
Isoetharine	0.34	++	++	–	3– 5	5– 20	60–150
Metaproterenol	0.65	+	+++	–	5–15	10– 60	60–180
Terbutaline	0.20	+	++++	–	5–30	60–120	180–360
Albuterol	0.09	+	++++	–	5–15	60– 90	240–360
Bitolterol	0.37	+	++++	–	5–10	60– 90	300–480
Pirbuterol	0.20	+	+++	–	5–10	40– 60	180–240
Ipratropium	0.18	–	–	++++	5–15	60–120	240–480

From Ferguson and Cherniak [11].

¹ The number of plus signs denotes the relative level of activity.

Table 5. Factors that might affect theophylline dosage requirements

	Larger theophylline dosage required	Small theophylline dosage required
Major change (26–50%)	cigarette smoking phenytoin rifampin isoproterenol i.v. phenobarbital carbamazepine aminogluthethimide	hepatic insufficiency heart failure cor pulmonale viral pneumonia cimetidine mexiletine ciprofloxacin, other quinolones allopurinol erythromycin influenza vaccination triacycloandomycin (TAO) propranolol oral contraceptives
Lesser change (10–25%) ²	low carbohydrate, high protein diet charcoaled food isoniazid ketoconazole	verapamil nifedipine tetracycline hydrocortisone aluminum hydroxide magnesium hydroxide thiabendazole

From reference 1.

¹ When increasing dosage, serum levels must be used for guidance.

² Data supporting these changes are less well documented.

longer-acting formulations provide 12-hour coverage and in some individuals allow a less disturbed night.

Anticholinergics

Ipratropium administered by inhalation is at least as effective (and possibly slightly more) than a β_2 -agonist, with fewer side-effects [20, 22]. Being slower in onset it does not lend itself for rescue but is generally administered as 2–4 puffs (20 μ g/puff) 4- to 6-hourly. The regular use of inhaled aerosols of ipratropium does not influence the rate of decline in FEV₁. It is customary to use both a β -agonist and an anticholinergic in the management of COPD. Combination products facilitate combined usage and are favoured by some. Other physicians prescribe an anticholinergic for regular use and recommend a β_2 -agonist as needed.

Theophylline

Theophylline preparations, especially those that are taken only once a day, may add further bronchodilation to the medications administered by metered dose inhalers [23]. Theophylline toxicity should be avoided. There are a variety of factors (including viral infections, smoking and many medications) that might affect the metabolism of theophylline and therefore the dosage requirements of theophylline products should be monitored. Since there may be a need to adjust (increase or reduce) the theophylline dose it is useful to be aware of some of these conditions (table 5). When established on theophylline, patients generally seem to benefit from it and are reluctant to discontinue its usage. In part this may relate to the other described actions of theophylline such as central stimulation and

respiratory muscle stimulation as well as its diuretic and anti-inflammatory properties.

Corticosteroids

Corticosteroids are useful during acute exacerbations and should be given as a short course starting at a high dose (e.g. 40 mg prednisone per day) and tapering over 10–14 days after which they should be discontinued completely. Only a small percentage (10–20%) of stable patients respond to oral steroids [10, 14, 20]. In such patients the risks of multiple side-effects from chronic oral steroid administration must be balanced against the relatively small gains in airflow which rarely translate into improvements in functional exercise capacity or health-related quality of life. Inhaled steroids may result in a response in a small percentage of those who responded to oral steroids. Although frequently prescribed for individuals with COPD, there is in fact very little evidence that stable patients derive any clinically meaningful benefits from ongoing inhaled steroid administration. As these medications represent potentially huge profits for the pharmaceutical industry it is very likely that the results of large multi-centre studies on the use of inhaled steroids will become available within the next few years.

Antibiotics

If bacterial infection is considered to be likely then a course of a broad-spectrum antibiotics (often in conjunction with a course of steroids) may be appropriate. Ideally there should be evidence of infection (leucocytosis, elevated temperature, radiographic change or sputum culture). However, short courses of antibiotics are often prescribed based on clinical impression [24]. It is there-

Table 6. Entry and exclusion criteria for the continuous or nocturnal oxygen therapy trial

<i>Entry criteria</i>
Clinical diagnosis of chronic obstructive lung disease
Hypoxaemia
PaO ₂ ≤ 55 mm Hg
PaO ₂ ≤ 59 plus one of the following:
Oedema
Haematocrit >55%
P pulmonale on ECG: 3 mm in leads II, III, aVf
<i>Lung function</i>
FEV ₁ /FVC ≤ 70% after inhaled bronchodilator
TLC ≤ 80% predicted
Age >35
<i>Exclusion criteria</i>
Previous O ₂ therapy: 12 h/day for 30 days during previous 2 months
Other disease that might be expected to influence mortality, morbidity, compliance with therapy, or ability to give informed consent
From Kvale et al. [25].

fore recommended that standard, less costly antibiotics be used and the newer, more expensive antibiotics be held in reserve for more specific indications.

Oxygen Therapy

Two classic multi-centre studies [25, 26] have shown that supplemental oxygen delivered for most of the 24-hour day is effective in reducing the mortality among patients with COPD who have resting hypoxaemia. In a study reported by the Nocturnal Oxygen Therapy Trial Group 203 subjects were randomly allocated to either continuous oxygen therapy or 12 h of oxygen therapy, and followed for at least 12 months. Entry criteria (table 6) included a PaO₂ of less than 55 mm Hg or less than 59 mm Hg if accompanied by oedema, an increased haematocrit or ECG

evidence of pulmonary hypertension. Oxygen was administered to maintain the resting PaO₂ above 60 mm Hg with the flow increased by 1 litre/min for exercise and sleep. A variety of delivery systems were used and patient compliance was monitored. The average patient was 66 years of age and had severe airflow limitation (FEV₁ <30% predicted), a limited maximal exercise capacity (37 W), a resting tachycardia (93 bpm) and modest pulmonary hypertension (mean pulmonary artery pressure 29 mm Hg). The mean PaO₂ while breathing room air was 52 mm Hg and the mean PaCO₂ was 44 mm Hg. The mean sleep saturation was 84% on room air and 94% on oxygen. After 12 months 64 patients had died (41 nocturnal oxygen and 23 continuous oxygen), thus the 12-month mortality was 21% (4%) for nocturnal and 12% (3%) for continuous oxygen. Of the basic characteristics, only the haematocrit and the pulmonary vascular resistance showed changes dependent on the treatment regimen. Haematocrit values fell more in patients on continuous oxygen than in those on nocturnal oxygen. This was significant at 12 months, and at 18 months haematocrit values had fallen by 2% from the baseline for those on nocturnal oxygen but had decreased by 9% for those on continuous oxygen. The pulmonary vascular resistance was measured after 6 months at which time those on nocturnal oxygen showed a mean increase of 6.5% whereas those on continuous oxygen showed a mean decrease of 11%. In addition, several measures of quality of life and neuropsychological function improved when all patients were considered. The patients studied were likely to have been a representative of stable patients with COPD. The treatment groups were similar and the treatment was shown to have achieved its short-term goal of reducing mortality and improving quality of life.

Fig. 3. Mortality in male patients. Smooth curves (straight line) indicate expected proportions surviving a constant risk of 12%/annum among the treated patients and (hatched line) 29%/annum among the controls [26].

In a second classic study the British Medical Research Council [26] reported the results of a three-centre prospective, randomized controlled trial established to determine whether oxygen given for 15 h/day over 3 years could reduce mortality among 87 subjects with severe airways obstruction, hypoxia (PaO_2 51 mm Hg) and moderate pulmonary hypertension (mean PAP 34 mm Hg). This study differed from the previous study in that subjects were hypercapnic (mean PaCO_2 54 mm Hg). Subjects were randomized to receive oxygen for 15 h a day or no oxygen. In those receiving oxygen the PaO_2 was kept above 60 mm Hg. In the treated group, 19 of the 42 patients died but in the control group 30 of the 45 patients died. Of note, this study reported different mortality patterns between men and women. In men, the mortalities of the treated and control

groups (fig. 3) were similar for the first 500 days after which the groups diverged with mortalities of 12% per annum in the treated group and 29% per annum in the control group. Women showed an unexpectedly divergent pattern of mortality from the onset of the study (fig. 4), but the smaller number of women (21 out of 87) made more detailed analysis difficult. Of the variables measured, a combination of red cell mass and PaCO_2 while breathing room air provided the best discriminant between those men who survived for 500 days and those who died within this period. Those subjects in whom the red cell mass plus the PaCO_2 exceeded 98 had a higher mortality at 500 days (61 versus 17%). The study failed to confirm that long-term oxygen could reduce established pulmonary hypertension but the treatment did appear to prevent a further rise in total pulmonary vas-

Fig. 4. Mortality in female patients. Smooth curves (straight line) indicate the expected proportions surviving at a constant risk of 5.7%/annum among the treated patients and (hatched line) 36.5%/annum among the controls [26].

cular resistance in the treated group as compared with the control subjects. The report concluded that further studies were needed to clarify which patients would be most likely to benefit from supplemental oxygen and to establish whether in those who are less hypoxic supplemental oxygen might prevent progression of their disease to cor pulmonale and premature death.

These studies have been very valuable in establishing a scientific basis for prescribing supplemental oxygen. They have also given rise to a substantial industry focused on promoting supplemental oxygen under a variety of circumstances not always supported by scientific information. The mechanism of improved survival appears to relate to a reduction in pulmonary vascular pressure, and cardiac work and an improvement in tissue oxygen delivery. It remains to be precisely delineated. There are important outstanding issues

related to the role of supplemental oxygen for individuals who, at sea level, are normoxic at rest ($\text{SaO}_2 > 90\%$). To date, improved survival has not been documented among those with only night-time hypoxaemia or those for whom hypoxia is exercise-induced. Long-term clinical trials are underway to better define the role of supplemental oxygen in these situations. A variety of methods of delivering supplemental oxygen (liquid, high pressure cylinders, concentrators) has assisted user convenience for both stationary and ambulatory circumstances (tables 7–9). Coupling the delivery system with mechanical or electronic conserving devices promotes portability by increasing the duration of the supply. Such devices are becoming readily available [27].

Table 7. Equipment for oxygen supply

Apparatus	Weight, lb	Performance
<i>Membrane sieves</i>		
PVO2D (DeVilbiss)	46	93% O ₂ at 3 litres/min
MC44D (DeVilbiss)	48	90% O ₂ at 5 litres/min
H-300 (Healthdyne)	40	90% O ₂ at 3 litres/min
BX-5000 (Healthdyne)	53	90% O ₂ at 5 litres/min
DC-100 ^a (Roman)	29	93% O ₂ at 2 litres/min
AC-300 ^a (Roman)	34	93% O ₂ at 3 litres/min
Emperor (Roman)	49	93% O ₂ at 5 litres/min
Mobilaire III (Invacare)	51	94% O ₂ at 3 litres/min
Mobilaire V (Invacare)	54	94% O ₂ at 5 litres/min
Spirit (Kee-Ox)	46	93% O ₂ at 3 litres/min
Elite (Kee-Ox)	56	90% O ₂ at 5 litres/min
429a (Puritan Bennett)		92% O ₂ at 4 litres/min
590 (Puritan Bennett)		90% O ₂ at 5 litres/min
<i>Membrane separators</i>		
Oxycare	35	45% O ₂ at 10 litres/min
OE Plus (Gulfstream)	68	40% O ₂ at 6 litres/min

Values of % are $\pm$ 3%. From Cooper [27].
^a Samsonite suitcase.

Table 8. Equipment for oxygen supply

Apparatus	Weight lb	Capacity litres	Performance
<i>Liquid</i>			
Walker (Linde)	6.5	–	4.0 h at 2 litres/min
C-1000 (Puritan Bennett)	7.5	–	8.5 h at 2 litres/min
C-T (Puritan Bennett)	8.4	–	–
OMS I (Pulsair)	7.5	400	10.0 h at 2 litres/min
OMS II (Pulsair)	10.3	824	23.0 h at 2 litres/min

From Cooper [27].

Respiratory Rehabilitation

In the last decade a number of clinical trials [28–30] have demonstrated that rehabilitation programmes are a useful adjunct in the management of patients with moderate or severe COPD. Such programmes are effective in both

the institutional and community setting. Rehabilitation programmes will address the above principles of management to which they add patient and family education, supervised exercise training and psychosocial support. Even small improvements in measured exercise tolerance may result in substantial gains

Table 9. Equipment for oxygen supply

Apparatus	Weight lb	Capacity litres	Performance
<i>Cylinders</i>			
H-size	150.0	6,840	57.0 h at 2 litres/min
G-size	–	3,600	–
F-size	–	1,360	–
E-size	17.0	680	5.0 h at 2 litres/min
E-size (aluminum)	13.0	680	5.0 h at 2 litres/min
E-size (Oxymatic)	–	680	40.0 h at 2 litres/min
D-size	–	420	3.5 h at 2 litres/min
D-size (Oxymatic)	–	420	3.5 h at 2 litres/min
C-size	–	240	2.0 h at 2 litres/min
C-size (Aluminum)	10.0	240	2.0 h at 2 litres/min
C-size (Oxymatic)	–	240	14.0 h at 2 litres/min
Mini (Oxylite)	4.0	–	9.5 h at 2 litres/min

From Cooper [27].

Table 10. Primary results of the meta-analysis

Outcome measures	Number of trials	Total number of patients (treatment/control)	Overall effect (95% CI)	
			effect size SD units	treatment effect natural units ¹
Maximal exercise capacity	11	160/149	0.3 (0.1–0.6)	8.3 W (2.8–16.5)
Functional exercise capacity	11	211/202	0.6 (0.3–1.0)	55.7 m (27.8–92.8)
Dyspnoea	6	126/108	0.8 (0.5–1.2)	1.0 (0.6–1.5)
Fatigue	4	111/ 96	0.6 (0.3–0.8)	0.8 (0.4–1.0)
Emotional function	4	111/ 96	0.5 (0.2–0.8)	0.6 (0.2–1.0)
Mastery	4	111/ 96	0.6 (0.4–0.9)	0.8 (0.5–1.2)

From Lacasse et al. [31].
¹ Natural units are those of individual items (7-point scale) of the Chronic Respiratory Disease Questionnaire (dyspnoea, fatigue, emotional function and mastery), an incremental cycle ergometer test (maximal exercise capacity), and a 6-min walk test (functional exercise capacity).

in health-related quality of life. Recognition of the importance of valid, reproducible, interpretable quality of life scales has been most helpful in identifying the optimum methods of addressing rehabilitation and of subsequently maintaining the benefits achieved during the

intensive phase. An essential component of any rehabilitation programme is exercise training for 4 weeks, at least 3 times a week for a duration of 30–40 min [31, 32] (table 10). The intent is to promote flexibility, strength and endurance. In some patients with mild to

Table 11. Indications for hospitalization of patients with COPD

1	Patient has acute exacerbation characterized by increased dyspnoea, cough or sputum production, plus one or more of the following: <ul style="list-style-type: none">– Inadequate response of symptoms to out-patient management– Inability to walk between rooms (patient previously mobile)– Inability to eat or sleep due to dyspnoea– Conclusion by family and/or physician that patient cannot manage at home, with supplementary home care resources not immediately available– High-risk co-morbid condition, pulmonary (e.g. pneumonia) or non-pulmonary– Prolonged, progressive symptoms before emergency visit– Altered mentation– Worsening hypoxaemia– New or worsening hypercarbia
2	Patient has new or worsening cor pulmonale unresponsive to out-patient management
3	Planned invasive surgical or diagnostic procedure requires analgesics or sedatives that may worsen pulmonary function
4	Co-morbid condition, e.g. severe steroid myopathy or acute cerebral compression fractures, has worsened pulmonary function
Other indications for hospitalization may apply to patients undergoing pulmonary rehabilitation.	
From reference 1.	

moderate levels of impairment cardiovascular training will occur but in many their level of impairment is such that dyspnoea limits their exercise tolerance at relatively low levels of power. Programmes in rehabilitation recognize that the primary respiratory impairment may be irreversible but that secondary generalized deconditioning and psychosocial sequelae may be reversed. Despite a large number of clinical trials there has been insufficient evidence to support respiratory muscle train-

Table 12. Indications for ICU admission of patients with acute COPD exacerbation

1	Severe dyspnoea that responds inadequately to initial emergency therapy
2	Confusion, lethargy or respiratory muscle fatigue (the last characterized by paradoxical diaphragmatic motion)
3	Persistent or worsening hypoxaemia despite supplemental oxygen or severe/worsening respiratory acidosis (pH <7.30)
4	Assisted mechanical ventilation is required, whether by means of endotracheal tube or noninvasive technique
From reference 1.	

ing as part of a rehabilitation programme. It also appears unlikely that ongoing nocturnal mechanical support will confer lasting benefit for patients with COPD although preliminary trials (most of which have been uncontrolled) would point to a possible role for a brief period of non-invasive ventilation if respiratory failure is thought to be consequent upon a reversible cause.

In-Patient Management of COPD

It is sometimes difficult to appreciate whether a patient with COPD requires acute hospitalization. Both the American Thoracic Society statement on the ‘Standards for the Diagnosis and Care of Patients with Chronic Obstructive Pulmonary Disease’ [1] and a recently published European workshop on COPD [2] include comments on in-patient management. Indications for admission depend at least in part on the available resources within an institution including the existence of personnel and equipment for more intensive care. Table 11 summarizes the indica-

tions for hospitalization of patients with COPD and table 12 summarizes the indications for ICU admission of patients with acute COPD exacerbations. It is beyond the scope of this article to address those issues in greater depth and readers are recommended to review the consensus guidelines suggested by experts in the field.

Conclusion

In this overview I have drawn attention to some of the key points in the clinical presentation and management of patients with COPD. For reasons of space, it has been impossible to

address many exciting developments such as nutritional or hormonal support, non-invasive ventilation, surgical approaches such as lung volume reduction or lung transplantation, etc. It has however become clear that in recent years our understanding of the pathophysiology clinical presentation and responsiveness of the condition has markedly influenced our choice of management. The careful application of a comprehensive management approach is likely to influence impairment, disability and handicap and to improve both functional exercise capacity and health-related quality of life among many individuals affected by COPD.

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