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Respiratory Medicine symposium

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ABSTRACT The Respiratory Medicine symposium considered many topics including the difficulties of managing functional breathlessness and breathlessness in pregnancy, pigeon fancier's lung, interventional bronchoscopy, inhalation therapy for COPD, pulmonary rehabilitation, and terminal care in non-malignant respiratory disease. The Robert W Philip Memorial Lecture focused on advances in the acute respiratory distress syndrome.

KEYWORDS Advances, breathlessness, evidence, investigation, management

LIST OF ABBREVIATIONS Acute lung injury (ALI), acute respiratory distress syndrome (ARDS), bronchoalveolar lavage (BAL), chronic obstructive pulmonary disease (COPD), cystic fibrosis (CF), extrapulmonary ARDS (ARDSexp), forced expiratory volume in one second (FEV1), pulmonary ARDS (ARDSp), pulmonary rehabilitation (PR), transitional dyspnoea index (TDI)

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EDITOR'S NOTE

The Respiratory Medicine symposium held in the College in November 2003 examined a wide range of respiratory diseases. Abstracts of individual presentations at the symposium have been published in *The Journal*,[1] but readers, particularly those with a general medical interest in respiratory disease, will appreciate Dr Michael Gibbon's thoughtful and well-referenced overview of the meeting.

ROBERT W PHILIP MEMORIAL LECTURE: ADVANCES IN ACUTE RESPIRATORY DISTRESS SYNDROME

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Acute respiratory distress syndrome is defined clinically by refractory hypoxaemia in association with bilateral pulmonary infiltrates on a chest radiograph with no evidence of elevated left atrial pressure, in the presence of a known precipitating factor for the syndrome. Both ARDS and its less severe manifestation, ALI, are responsible for considerable morbidity and mortality amongst the critically ill.

In 1967, ARDS was described in a cohort of 12 patients.[2] The patients had different causes of ARDS, but had in common tachypnoea, hypoxaemia, reduced lung compliance, and no response to 'usual' therapy. The syndrome was then defined by the American-European Consensus Conference as a 'syndrome of inflammation and increased permeability (of the capillary membrane) that is associated with a constellation of clinical, radiological, and physiological abnormalities that cannot be explained by, but may co-exist with, left atrial or pulmonary hypertension'.[3]

The epidemiology of the syndrome is much more complex than was originally thought. Establishing the precise incidence of the syndrome is difficult as there was only widespread acceptance of the disorder as a distinct entity in 1994 and prior to that differing terminology was used to describe it. Established ARDS probably has an incidence of 5–15 per 100,000 per year. It is clear now that the nature of the precipitating condition is important. The presentation quoted the incidence of ARDS at around 20% in trauma patients, higher in patients with sepsis and higher still, at around 60%, in patients with septic shock. The incidence in patients undergoing cardiopulmonary bypass was quoted at about 1%.

Acute respiratory distress syndrome is classically divided into three overlapping phases that correlate with the clinical evolution of the disease. These are the exudative phase of oedema and haemorrhage, the proliferative phase of organisation and repair, and the fibrotic phase.

The exudative phase[4] is characterised by diffuse alveolar damage. It usually occurs during the first week after the onset of respiratory failure. Plasma proteins and cell debris leak through the damaged endothelial–epithelial barrier into the alveolar space. Endothelial injury is present but not severe. Neutrophils congregate within the alveolar space. In contrast to the endothelium, there is extensive necrosis of type I alveolar epithelial cells which slough from the alveolar surface and are replaced by hyaline membranes. Type II epithelial cells, which

secrete surfactant, are more robust and provide a population of cells which are thought to replicate and differentiate to replace the type I cells. This begins as early as the third day after the onset of ARDS and heralds the beginning of the proliferative phase.

The proliferative phase[4] is characterised by organisation of intra-alveolar and interstitial exudates. Rows of type II cells differentiate and cover the basement membrane to replace the lost type I cells. Within the alveolar wall fibroblasts and myofibroblasts proliferate. They then migrate through defects in the alveolar basement membrane into the fibrinous intra-alveolar exudate converting it into cellular granulation tissue and ultimately into fibrous tissue. This exudate retains fluid and acts as a scaffolding through which leukocytes and fibroblasts migrate and ultimately transform into connective tissue. Within the alveolar wall, fibroblasts cause septal fibrosis. In addition, collapse of damaged alveolar walls is followed by a process termed 'collapse induration' where alveolar walls become sealed in apposition by organising fibrin and hyperplastic epithelium. This results in fewer but larger alveoli with dilated alveolar ducts.

The fibrotic phase[4] is the last of the three phases. Histologically it can occur as early as the first week after the onset of ARDS. There is an increase in total lung collagen and macroscopically the lung parenchyma is pale and spongy, consisting of areas of microcystic air spaces and irregular scarring. If ARDS becomes chronic, healed abscesses and chronic interstitial emphysema cause larger cysts.

The nature of the precipitating condition affects the outcome in ARDS. In trauma patients the presentation alluded to the idea that the relatively low incidence of ARDS probably in part reflects the young American cohort affected. Comparatively, the outcome is substantially worse in patients with sepsis; there is a mortality of up to 40–50%. It is now clear that ARDS can be divided into two pathogenetic pathways depending on whether the insult on the lung is direct (ARDSp), or indirect (ARDSexp). In a study looking at the mechanics of the lung measured at differing values of positive end-expiratory pressure a differing response was found between the two groups.[5] This suggested that oedema and collapse are more important in ARDSexp, and that consolidation is more important in ARDSp.

Significant advances have been made in understanding the pathophysiology of ARDS. Early work found that levels of interleukin-8, a neutrophil chemo-attractant, were elevated in blood and BAL fluid of patients who subsequently went on to develop ARDS,[6] suggesting the importance of neutrophils in the pathogenesis of ARDS. Subsequent studies have shown that interleukin-8 concentrations and alveolar neutrophil counts in patients with ALI/ARDS are significantly different in patients with ARDSp compared to ARDSexp, suggesting a slightly different pathogenesis for each.

It is apparent that oxidative stress, in generating free radicals, plays a role in the modulation of the inflammatory response as shown by the increased levels of thioredoxin in blood and BAL fluid from patients with ALI/ARDS (unpublished data). This may become a target for intervention in the future. KL-6 is a mucin-like protein strongly expressed on type II epithelial cells. Serum levels of KL-6 are elevated and correlate with disease activity in pulmonary inflammation, as shown in work on sarcoidosis.[7] Recent data have shown that KL-6 concentrations are elevated in patients with ARDS compared with ventilated or healthy controls, and have some significance in predicting survival in these patients.[8]

In patients with ARDS it is imperative to manage the underlying precipitant at the outset and to look for and treat complicating infection. Computerised tomography scanning can be helpful as an adjunct in management by excluding unidentified co-morbidities, and may also help us understand the transition in these patients from inflammation to fibroproliferation.

Management of ARDS can be divided into three strands Respiratory support; Non-respiratory support; and Specific therapies. Recent advances relevant to each of these as mentioned by the speaker are now described in more detail.

Respiratory support

It is becoming clear that the use of lower tidal volumes in this group of patients is associated with a reduction in mortality as compared with higher tidal volumes,[9] although more research is needed.

Use of the prone position during mechanical ventilation has been shown to improve oxygenation, and although this does not translate into improved survival,[10] it should be considered in patients in whom oxygenation is proving difficult. It undoubtedly has practical problems in terms of preventing pressure necrosis especially around the face and neck.

The use of extracorporeal gas exchange in ARDS is still an area of controversy and further results are awaited.[11]

Non-respiratory support

Fluid balance is critical in ARDS. In a condition in which there is increased alveolar capillary permeability flooding the lungs with fluid is a real possibility. By contrast keeping the patient very dry and reducing cardiac output will diminish oxygen delivery to the tissues and arguably increase multiple organ dysfunction. For this reason a

large multicentre study is currently comparing fluid restriction vs fluid replacement in ARDS.

Enteral nutrition is important in the management of ARDS. It does not have the disadvantages of total perenteral nutrition such as expense and catheter-related infection, and has the advantages of increased blood flow, improved barrier function (decreasing translocation of bacteria and their toxins) and a decreased incidence of stress ulceration.[4] There are also preliminary data to suggest that using so-called 'immunomodulatory feeds,' which contain glutamine and other anti-oxidants, decreases neutrophil recruitment as measured in BAL fluid, improves oxygenation and possibly shortens mechanical ventilation time.[12]

Specific therapies

Surfactant will probably be used in this field in the near future. Preclinical and clinical data already exist, but currently its exogenous administration has proven inconsistent as a therapeutic modality in patients with ARDS.[13]

Steroids were used in very early studies in high doses within 24 hours of the development of ARDS and showed no survival advantage.[14] There is currently an American Thoracic Society-sponsored study looking at the effects of steroids when used after 10 or 11 days, during the fibroproliferative stage of the disease, to determine whether they assist in recovery and resolution of inflammation. The evidence-base regarding steroids at present is insufficient to allow any firm recommendations to be made, but the results of the above study are eagerly awaited.

The use of stem cells in ARDS is an exciting area. It is envisaged that donor bone marrow-derived stem cells could be infused intravenously into patients with ARDS. The stem cells could then undergo differentiation into endothelial cells and be targeted to the damaged lung where they would help restore the lung capillary network. A better understanding of stem cell biology is needed, but it is a potential clinical application with substantial implications.

In the decade since ALI/ARDS was first given a unifying definition there has been considerable change in our understanding of its pathogenesis and treatment. The original definition was relatively simple with a subsequent omission of exclusion criteria. It assumed that patients fulfilling criteria for ALI progressed to ARDS. As a result patients with different pathologies were included and 'misclassified' as having ARDS. Furthermore the nature of the underlying cause was not taken into account, i.e. ARDSp vs ARDSexp. On this basis, it is believed, that the time has come for there to be revision of the definition of ARDS and this is currently in progress.

In conclusion, the definition of ARDS must change and better studies are needed. There have however been considerable advances in our understanding of the pathophysiology of the disease and it is clear that supportive care should not merely be in the form of ventilation. Intervention will likely become protocol driven, concentrating on repair (for example using stem cells) as well as support.

FUNCTIONAL BREATHLESSNESS

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Medically unexplained or functional symptoms are common. In a retrospective review of 971 consultation episodes with frequent attenders, 21% of the consultations were medically unexplained.[15] Different collections of symptoms characterise disorders of uncertain aetiology in separate specialties (e.g. irritable bowel syndrome, fibromyalgia, temporomandibular joint disorder, non-cardiac chest pain). Interestingly, many symptoms overlap each of these syndromes and as such the same patient may be diagnosed as having many such syndromes depending on which clinics they have attended. These conditions are often chronic and associated with significant disability.

'Functional breathlessness' is an example of such a condition that presents to the respiratory physician. Up to 14% of patients presenting to a respiratory specialist with breathlessness will have no organic cause identified.[15] These patients will often be labeled as having functional breathlessness. Before making such a diagnosis, organic disease must be excluded.[16] In breathless patients with normal clinical examination, chest radiograph and spirometry the differential diagnosis is still extensive. For example, in patients under 40 presenting with intermittent breathlessness and a normal arterial-alveolar gradient the diagnosis of asthma should be considered. Monitoring of peak flows or a trial of inhaled therapy may be appropriate. It should be noted that up to 10% of patients with asthma also have panic disorder.

Primary pulmonary hypertension and occult pulmonary embolism can also be the cause of previously unexplained breathlessness in the relative absence of signs or spirometry abnormalities. It is therefore important to exclude these organic causes of breathlessness before a diagnosis of functional breathlessness is made.

In the management of medically unexplained syndromes it is important to set an appointment time of the appropriate length, to listen to the patient and not to doubt their symptoms. Clinics are best run jointly or in close collaboration with a psychiatrist. Useful

treatments include cognitive behaviour therapy, graded exercise therapy, education about the role of the autonomic nervous system in producing many of the symptoms, and relaxation therapy.[17] Specific breathing exercises are especially useful in patients who also have panic disorder.[17]

THE BREATHLESS PREGNANT LADY

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Breathlessness is a very common symptom in pregnancy. It is also a very non-specific symptom and can be the manifestation of normal physiological changes. During pregnancy the functional residual capacity is reduced by 17–20%.[18] Breathlessness also occurs as a result of increased sensitivity of the brain to progesterone which leads to hyperventilation and a compensated respiratory alkalosis.[18]

A sudden change in breathlessness cannot be explained on the basis of physiological change and requires thorough assessment and appropriate investigations. It is much harder to determine the clinical significance of insidious breathlessness during pregnancy.

In investigating the breathless pregnant lady the worry for the patient, and often the clinician, is the potential effect on the foetus from exposure to radiation or from any medication administered. Chest radiography is therefore often avoided despite the fact that the radiation dose is small. To put this in perspective a single chest radiograph generates only half of the radiation that can be expected from a transatlantic flight. Perfusion lung scanning also carries a low risk to the foetus.[19] Computerised tomography pulmonary angiography is often avoided because of the theoretical increase in tumour susceptibility in the pregnant breast exposed to radiation.[20] The risk of this must be balanced against the risk to both mother and foetus from not investigating and treating pulmonary embolism. It must be emphasised that in general if a diagnostic procedure is deemed clinically necessary then it should be performed and the patient reassured accordingly.

Breathlessness during pregnancy may be classified according to: diseases with increased incidence during pregnancy; diseases occurring 'only' during pregnancy; and coincidental diseases causing breathlessness. These are outlined below:

Diseases with increased incidence during pregnancy

Thromboembolic disease occurs more commonly during pregnancy which is a hypercoagulable state.[21] This thrombogenic state is caused by the production of increasing amounts of clotting factors, diminished fibrinolysis, increased platelet turnover and venous compression by the uterus.

Treatment of acute massive pulmonary embolism with fibrinolytics is appropriate but must be done with caution because of the theoretical risk of foetal haemorrhage. Low-molecular-weight heparin should be used in preference to unfractionated heparin because there is a reduced risk of heparin-induced thrombocytopenia (1% vs 3%) and foetal osteoporosis.[22, 23] It should be noted that the anticoagulant effect should be checked during pregnancy as the dose required is usually higher than that calculated by weight in non-pregnant patients. Warfarin should be avoided where possible in the first trimester because it can cause congenital malformations.[23]

Diseases occurring only during pregnancy

Ovarian hyperstimulation syndrome is usually an iatrogenic complication of ovulation-induction therapy. Spontaneous cases have been reported during pregnancy in rare instances.[24] Its most severe form is characterised by the formation of multiple ovarian cysts induced by fertility treatment and sustained by subsequent pregnancy, causing massive ovarian enlargement. The ensuing fluid shifts result in extravascular fluid accumulation and intravascular volume depletion with resultant renal failure, hypovolaemic shock and in some cases death.[24]

Amniotic fluid embolism may occur during or soon after labour as a result of vigorous uterine contraction. It is very rare with an incidence of approximately 23 per million maternities and a mortality rate of 16% for reported cases.[25] In the UK, it accounts for 8% of maternal deaths.[25]

Coincidental diseases causing breathlessness

The effect of pregnancy on asthma is unpredictable but is probably reflected by the 'rule of thirds': one-third of patients with pre-existing asthma get better during pregnancy, one-third get worse and one-third stay the same.[26] Patients with asthma should be reassured that pregnancy is unlikely to be affected by medication used for control. All the drugs commonly used to treat asthma, including short and long-acting β2-agonists, inhaled corticosteroids, and methyl xanthines are safe in pregnancy. Oral corticosteroids have been shown to cause cleft lip and cleft palate in animal studies but an increased risk has not been demonstrated in humans. It is widely accepted that lack of treatment is more of a risk to the mother and fetus than are the side-effects of asthma treatments.

Prevailing concerns about side-effects of treatments are highlighted by studies suggesting that pregnant women are less likely to receive appropriate treatment for acute asthma in A&E departments compared to non-pregnant women.[27]

There is no evidence for an increase in pulmonary infection in pregnancy despite the fact that there is some immune suppression particularly in the second and third trimesters.[28]

The outcome of pregnancy in patients with CF probably relates to lung function.[29] Attempts to conceive should probably be avoided where the FEV1 is less than 50% predicted[29] and where there is pulmonary hypertension or cor pulmonale.[30] When pregnancy does occur there should be close contact between an experienced obstetrician and a chest specialist with a special interest in CF. Chest infections should be treated aggressively, nutritional support should be optimised, close attention should be paid to physiotherapy and there should be close monitoring for diabetes.[29]

PIGEON FANCIER'S LUNG

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This condition is a form of hypersensitivity pneumonitis caused by exposure to pigeon bloom. The classical presentation is with breathlessness, malaise, unproductive cough, fever and sweating. Clinical signs characteristic of the condition are pyrexia, tachypnoea and inspiratory lung crackles. Symptoms usually manifest themselves within 4–8 hours of antigen exposure[31,32] and symptoms may be present in up to 16% of exposed subjects.[32]

Acute and chronic forms of the condition can be characterised partly by pulmonary function tests. Acute forms lead to a restrictive ventilatory defect, hypoxaemia with hyperventilation and a reduced transfer factor. Chronic disease leads to small lungs, airway obstruction and a reduced transfer factor.

A recent study[33] has identified six significant predictors of hypersensitivity pneumonitis. Pigeon fancier's lung was one of the predominant subgroups in the patients analysed. The predictors are: exposure to a known offending antigen, positive precipitating antibodies to the offending antigen, recurrent episodes of symptoms, inspiratory crackles on physical examination, symptoms occurring 4–8 hours after antigen exposure, and weight loss.[33]

A commonly held belief is that identification of precipitating antibody (IgG) to the pigeon bloom antigen merely indicates exposure. The presentation robustly challenged this assertion. Antibody expression is closely linked to inflammatory activity and may have an important role in pathogenesis.[32] Antibody can be detected in asymptomatic subjects and its presence therefore is not sufficient to make a diagnosis,[32] however physiological changes can be detected in such patients.[34] It has been demonstrated that the titre of IgG antibody is correlated with a spectrum of disease severity including subclinical disease.[35]

There appears to be a genetic predisposition to pigeon fancier's lung. The susceptibility genes are associated with the loci for HLA-DR736 and HLA-B837. In order to develop the disease, susceptible patients require inhalation of the finely dispersed particles. There is a consequent stimulation of a hypersensitivity reaction with granulomatous inflammation. As smoking reduces the IgG response to inhaled antigens and impairs macrophage function it is not surprising that hypersensitivity pneumonitis is significantly less common in smokers.[38]

All patients with pigeon fancier's lung should be considered for some form of intervention. Exposure to pigeons should be reduced by minimising handling. Antigen load can be reduced by use of an effective specification mask (EN149:FFP1(S)) and replacement filters (EN143:1990).

Oral steroids can be used to control the immune reaction. The presentation recommended prednisolone 40 mg daily for three weeks, reducing by 5 mg weekly until reaching 15 mg daily, and then continuing with this dose for at least three months before consideration of reduction. High dose inhaled steroids can be considered thereafter for long-term maintenance. Response should be monitored using symptoms, pulmonary function testing and measurement of C-reactive protein and specific precipitating antibody levels.

Pigeon fancying is a major obsession and big business. Every year up to 12,000 people attend the Winter Gardens in Blackpool for a major pigeon fancier's show. It is vital to understand that people are very reluctant to change or give up this commitment without compelling reasons. Indeed an editorial in the Pigeon Racing News and Gazette once stated that pigeon fancier's lung is a 'non-existent complaint which exists only in the imagination of daft doctors'![39] Clinical management therefore requires an approach which is both sensitive and understanding.

INTERVENTIONAL BRONCHOSCOPY

Dr Phil Barber, Consultant Respiratory Physician, North West Lung Centre, Wythenshawe Hospital, Manchester, England

Many of the symptoms of bronchial carcinoma are caused by tumour arising in and obstructing a major airway. These symptoms include cough, haemoptysis, breathlessness and infection secondary to collapse of a proximal airway. Many of these symptoms can be alleviated by treatment modalities using bronchoscopic techniques.

Physical debulking techniques, which can be used to relieve large airway obstructions, include electrocautery,

bronchoscopic surgery and laser photo-resection. Biological tumour-reducing techniques are also used such as endobronchial brachytherapy[40] and photodynamic therapy.[41]

Electrocautery employs alternating electrical current to produce coagulation and vapourisation of endobronchial lesions. Laser photo-resection produces a similar result but with use of a laser such as the Nd-YAG laser.

Endobronchial brachytherapy is a technique which involves the insertion of a catheter into a bronchus. This is then placed in close proximity to an endobronchial lesion. The catheter contains a radioactive source such as ^{192}Ir, which delivers radiation to the lesion. Single dose brachytherapy offers symptom palliation comparable to that obtained with standard fractionated external beam radiotherapy and also offers additional flexibility for combined treatment, re-treatment, and the synchronous treatment of bilateral primary disease.[42] In selected cases it is potentially curative in the treatment of small tumours.[43]

Photodynamic therapy involves the intravenous administration of a sensitising agent – a haematoporphyrin derivative – which is selectively taken up by tumour tissue. This compound fluoresces when exposed to light of the appropriate wavelength. Within 24–48 hours of administration, light of the appropriate wavelength is then shone onto the tumour for several minutes during bronchoscopy. The resultant chemical reactions cause selective death of malignant cells through the production of toxic oxygen radicals. This results in tumour regression in both progressive and relapsing disease.[44]

Tracheobronchial stenting is used to bypass tumours to allow for an increase in airway calibre without tumour reduction. It can be used in progressive or relapsing disease or be preparatory to definitive anti-tumour therapy. Many types of stent are available and some may be placed by a standard flexible bronchoscopy procedure without the need for radiological screening.

Fluorescence bronchoscopy[45] utilises the principal of autofluorescence. When the bronchial surface is illuminated by a blue light such as that from a helium-cadmium laser, there is a reduction in fluorescence intensity in tissue that is abnormal. The monitor used to view images from the bronchoscope displays this reduction; normal tissue appears green and pre-malignant or malignant lesions appear brown or red-brown. Diagnostic and potential treatment implications of fluorescence bronchoscopy remain uncertain, but the technique undoubtedly has a role in endobronchial staging and in the detection of early invasive disease.

The successful use of endobronchial therapy requires a multi-disciplinary approach. The many therapeutic options can then be considered and combined to provide patients with a management plan aiming to improve their long-term outcome or to help in the palliation of troublesome symptoms.

INHALED DRUG THERAPY FOR CHRONIC OBSTRUCTIVE PULMONARY DISEASE: THE EVIDENCE BASE

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Chronic obstructive pulmonary disease is a major cause of morbidity and mortality. Pharmacological therapy has relied largely on 'borrowing' therapies used in the treatment of asthma. It is clear that the side-effect profile is lower in drugs given by inhalation. However, the relative benefits of inhaled therapy have been uncertain until the last five years when a series of large clinical studies have described significant symptomatic improvements in the face of only modest changes in lung function.

In order to improve the overall treatment of COPD there is consensus that the development of guidelines is beneficial. Guidelines now exist at national (British Thoracic Society), international (European Respiratory Society, American Thoracic Society) and global levels (Global initiative for chronic obstructive lung disease). Objectives of COPD management must include prevention of disease progression, relief of symptoms, improvement of exercise tolerance, improvement in health status, prevention and treatment of exacerbations, prevention and treatment of complications, reduction in mortality and minimisation of the side-effects of treatment.

Treatment with inhaled short acting bronchodilators (β2-agonists, anti-cholinergics and combination) has been shown to produce improvements in FEV1 and the improvement seen is greatest using the combination of β2-agonist and anti-cholinergic.[46] However, we now know that this does not necessarily translate to improvement in symptoms. This is because FEV1 accounts for only 5% of the variance in patients' quality of life. Furthermore, the effect is only achieved for four to six hours and to maintain this improvement requires regular use of therapy which in practice does not always occur due to poor compliance. Long-acting bronchodilators, both β2-agonists such as salmeterol, and anticholinergics such as tiotropium, have been shown to produce an improvement in FEV1.[47] They are also effective in reducing the degree of breathlessness the patient experiences, as measured by a validated score known as the TDI,[48] and in reducing exacerbation frequency. These effects are well maintained over one year and are often accompanied by a reduction in the number of hospitalisations. Exercise performance also

improves significantly. This is due to lung volume changes rather than changes in expiratory flow.

Inhaled corticosteroids do not appear to reduce the rate of decline in FEV1,[49,50] and hence do not appear to affect disease progression. They do, however, reduce exacerbation frequency in patients with an FEV1 <50% predicted[51] and also reduce the rate of decline in health status.[50]

Treatment with a combination of a long-acting bronchodilator and inhaled corticosteroid produces larger effects than inhaled corticosteroid alone in terms of improvement in FEV1[52] and in perception of breathlessness (measured using the TDI).[52]

In conclusion, in stable COPD, sustained bronchodilatation reduces symptoms, exacerbations and health impairment. If exacerbations are frequent the addition of an inhaled corticosteroid should be considered if the FEV1 is less than 50% predicted. The optimal medication is yet to be defined.

PULMONARY REHABILITATION: WHERE TO NOW?

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Pulmonary rehabilitation is defined as 'a multi-disciplinary programme of care for patients with chronic respiratory impairment that is individually tailored and designed to optimise physical and social performance and autonomy'.[53] Despite the fact that there are about 900,000 people in the UK suffering from COPD only a tiny proportion have the opportunity to attend PR. Of 266 hospitals surveyed by the British Thoracic Society only 160 had some form of PR and only 86 had secure funding. The programmes available usually vary in their size and quality.

The necessary components of a PR programme include physical training in endurance and strength, education, psychological and behavioural input, relaxation and energy conservation, and nutrition. There is good evidence that PR is effective, leading to significant improvements in exercise capacity and breathlessness[54] as well as improvements in quality of life.[55] The effects on respiratory muscle training are, however, equivocal at present and the benefits of psychosocial support are not clear.[56]

How long are the benefits maintained?

A recent study has shown that while there were benefits in walking distance and quality of life at 12 months, the effects had waned by 24 months, but were still greater than they had been pre-rehabilitation.[57] Furthermore, it appears that repeated yearly programmes lead to similar short-term, but not additional long-term gains.[58]

Pulmonary rehabilitation can be delivered effectively at home[59,60] and in primary care[61] but is most commonly achieved in the UK in hospital outpatient departments. It has been shown that PR is cost-effective.[62]

In conclusion, there is a need to make PR more available by effective use of local facilities. The benefits may be prolonged if maintenance programmes are provided. Psychologists undoubtedly have much to offer both in terms of patient selection and in changing of exercise behaviour. Collaboration between primary and secondary care is imperative. It will allow for a larger number of patients to be able to access and gain benefit from pulmonary rehabilitation.

TERMINAL CARE IN NON-MALIGNANT, END-STAGE DISEASE – HOW CAN WE IMPROVE IT?

Professor S Ahmedzai, Professor of Palliative Medicine, University of Sheffield, Sheffield, England

Chronic obstructive pulmonary disease is associated with significant morbidity, particularly in its latter stages. Such non-malignant end-stage respiratory disease has been largely ignored by health services in stark contrast to advanced cancer. Most patients either die slowly in hospital wards, at home, or in nursing homes. Palliative care services are becoming more interested in patients with non-malignant terminal illness, but will have to expand in order to accommodate the massive associated workload.

Studies have shown that physical symptoms such as breathlessness, pain, cough, anorexia, constipation and nausea are common in chronic lung disease and are comparable with symptoms reported by patients with lung cancer.[63] Depression and anxiety are more common in patients with COPD than in lung cancer.[64] Quality of life measurements show that patients with COPD are affected as much as patients with lung cancer,[65] and because the duration of their illness is longer, the total period over which their quality of life is impaired is greater.

There is also evidence that communication with patients with COPD regarding the terminal nature of their illness is lacking.[64] Patients with long-term non-malignant disease are more likely to have reduced activities of daily living[65] and to have reduced services at their disposal.[64] Patients with COPD and their carers are less likely to receive care in their homes from district and specialist palliative care nurses than are patients with cancer.[64]

It is clear, therefore, that although the overall degree of physical and psychosocial hardship is comparable between patients with cancer and non-malignant disease, patients with cancer are more cared for.

Knowledge of the management of physical symptoms should be easily transferrable from cancer to non-malignant disease. However, myths and fears about the use of analgesic and sedating drugs are prevalent in the minds of public and professionals alike. Modern synthetic opioids such as oxycodone offer advantages over codeine and morphine for the control of breathlessness and pain, but randomised controlled trials of symptom control with these agents in patients with end-stage COPD are lacking.

It should be assumed that palliative care principles applied to patients with cancer and their carers can be transferred to non-malignant disease. Healthcare professionals are often wary of referring patients with non-malignant disease to palliative care services because of difficulties in judging prognosis. Studies in Sheffield have shown that both medical and nursing staff are unlikely to identify patients with COPD as having palliative care needs.[66, 67]

It may help to use a new approach towards the care of patients with COPD and their carers. This approach should be supportive and not restricted to the end of life. It will be determined by physical and psychosocial information, rehabilitation and existential needs. Supportive care embraces palliative care for the terminal stages of life, but if offered from the time of diagnosis, more patients may benefit from seamless and holistic care.[68]

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