Palliative Care of Respiratory Disease in Primary Care

62

Patrick White

Contents

Abstract

The palliative care of advanced progressive respiratory disease in the setting of a primary care team is concerned mainly with chronic obstructive pulmonary disease (COPD), idiopathic pulmonary fibrosis (IPF), and cystic fibrosis (CF). COPD is the commonest of these but it is perhaps the most difficult to identify in its final stages. IPF has a trajectory and prognosis more akin to malignant disease. Though relatively rare in general practice, IPF is the disease among these three that has the most easily definable terminal stage, and so primary care teams should be alert to the palliative care needs of these patients.

CF is a remarkable disease because life expectancy at birth with CF has changed from childhood or teenage years to 30 years now,

P. White (✉)
Primary Care Respiratory Medicine, School of Population Health and Environmental Science,
King's College London, London, UK
e-mail: Patrick.white@kcl.ac.uk

R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_61

and for those aged 30 years, life expectancy is now in mid-50s. Like COPD, prognosis in CF is difficult to define. Most people with advanced disease in both groups are living with the disease. Most of these people want to continue living in the face of considerable challenges. The task in both of these diseases is to develop an approach to the amelioration of symptoms and to the support of patients and carers, that is, in keeping with the personal objectives of the patients. Information about treatment, future exacerbations, and the risk of dying is all important. Symptom control is difficult, and for intractable breathlessness, oral morphine has a role in many patients.

End-stage progressive nonmalignant respiratory disease:

the challenge/the burden from a palliative care perspective/the symptoms/issues in specific diseases/ the assessment and treatment of breathlessness in respiratory disease

1 The Challenge

The palliative care of respiratory disease presents the classic challenges of advanced progressive nonmalignant disease. The disease trajectory is often prolonged and uncertain. The transition between high dependency and dying may be imperceptible. In idiopathic pulmonary fibrosis (IPF), the end stage of the disease may resemble the terminal stage of a moderately progressive cancer. As symptoms become intractable, their management can be increasingly complex, and multidisciplinary input is likely to be needed.

In this chapter, the focus is on the advanced progressive nonmalignant diseases of the respiratory system. Lung cancer will not be treated as a separate issue here because the features of the terminal stages of lung cancer are largely indistinguishable from other malignant diseases in which metastasis to the lung is prominent.

The two most common progressive respiratory diseases that present to palliative care are chronic obstructive pulmonary disease (COPD) and idiopathic pulmonary fibrosis (IPF). They lead to contrasting experiences and different demands. COPD is likely to have progressed over 10 or 20 years. It usually does not progress to a clear terminal stage of the disease. Death may be relatively sudden from a severe acute exacerbation or pneumonia. IPF is likely to be more predictably progressive. The mean survival of IPF from diagnosis is 2.5–3.5 years. It usually has a more defined terminal stage and a more conventional opportunity for palliative care intervention than COPD.

Cystic fibrosis (CF), an inherited condition, has an altogether different onset and trajectory, from early life until premature death, which is usually in the 1950s nowadays. The need for palliative care of cystic fibrosis has only recently been addressed in the research literature. Despite its systemic effects, particularly in the gastrointestinal tract, the greatest threat in CF is progressive respiratory disease. Death may be from an acute infection. Many patients are selected for possible lung transplantation when respiratory function has been severely impaired. At that point the need for palliative and supportive care input is not likely to be in the domain of primary care.

The palliative care of advanced progressive respiratory disease shares the same basic aims of all palliative care. Timely planning and provision of clear information are the cornerstones of treatment. Neither should depend on being able to make an accurate prognosis. Symptom palliation should be determined by the severity of the symptom and the responsiveness of the underlying pathology to the treatment. Involvement of the patient, and their carers, in decisions about their care will help to ensure that care is appropriate. Providing an accurate prognosis may be challenging. That difficulty should not be used as an excuse for failing to prepare patients and their families for what lies ahead.

In advanced progressive nonmalignant respiratory disease, particularly in COPD and in CF, living with the disease is the dominant issue. The risk of death, rather than preparation for it, is the shadow that requires acknowledgment. In IPF, by contrast, the prognosis, all too clearly, is short.

The context of the stage of the disease in chronic nonmalignant respiratory disease is

important to these discussions. For some clinicians, it may be more difficult to introduce this subject because of the greater uncertainty that exists over the disease prognosis. Acknowledgment that prognosis is not the key issue here may help. Putting the issue of prognosis to one side may allow clearer thinking to be done about the risks of the disease at this stage, including the risk of dying. Will it be useful for my patient if I raise the subject of the risks associated with their illness? Is my patient someone who would like to consider the risks that they face? Have they reached the stage that life has become precarious because of the risk that the next exacerbation will be fatal?

Symptom control is the second big challenge in advanced nonmalignant respiratory disease. Patients with advanced severe disease will survive at least 2 years on average. This is not the moment to exhibit all the drugs at the clinician's disposal in the attempt to ameliorate intractable breathlessness. There is a need for a careful structured approach to symptom palliation that adopts a realistic evaluation of the patient's position. This approach will be discussed more at length in the Sect. 3. At this point the clinician should review what has been provided so far.

In this chapter the prevalence, burden, and risk of death from respiratory disease is discussed from the perspective of primary care in the UK. The population of the UK is now more than 60 million people. Where figures for prevalence are given, readers should translate those to their own country or setting. Prevalence can vary significantly. The incidence of COPD, for example, is likely to fall progressively in the UK where rates of smoking have plummeted in the last 40 years to a low of 16%. Exposure to biomass fuels in the home is virtually unheard of in the UK. This contrasts to countries in which the promotion of cigarette smoking has continued unabated and biomass fuel is commonly used for cooking. In such circumstances death from COPD is likely to be much younger because the exposure to risk factors starts earlier in life.

This chapter is written for primary care, taken from the experience of primary care in the UK. It is not directed at a particular clinical group. The issues discussed should be as relevant to general practitioners or family physicians as they are to nurse specialists, practice nurses, community nurses, healthcare assistants, and other professional clinical groups caring for patients approaching the end of their lives in the community. In other countries the organization of healthcare may differ significantly from that in the UK. Readers should translate the ideas presented here to their own setting.

2 The Burden from a Palliative Care Perspective

2.1 Chronic Obstructive Pulmonary Disease (COPD)

COPD is common. About 2% (>1,000,000) of people have diagnosed COPD in the UK (British Lung Foundation 2018). Ten percent of these have very severe disease as defined by the spirometry criterion of forced expiratory volume in the first second (FEV_1) (White et al. 2013). The prevalence of COPD in the UK is based primarily on people who have symptomatic disease. The prevalence varies quite markedly from country to country depending on the cause of the disease and whether or not screening is carried out for COPD. In many of the people diagnosed with COPD through screening, the disease causes no symptoms and has no impact on quality of life at the time of screening.

In developed countries the main cause of COPD is tobacco smoking. Occupational exposures account for a small proportion of the prevalence. In countries with high rates of poverty or large rural communities, exposure to biomass fuels is a significant cause of the disease. Exposure to biomass fuels is usually through cooking with wood or animal waste. The cooking is done in the house with poor ventilation. The whole family is exposed to smoke and volatile materials from a young age.

About 30,000 people die from COPD in the UK every year, just under 1 death from COPD for every GP each year or 3–6 deaths for a primary care team per year. This depends on the number of

patients registered with the team. This is not far below the rate of deaths from lung cancer. The mean age of death from COPD in the UK is 76 years. Comorbidities are likely to contribute to the risk of death. They may complicate the care of people with advanced COPD.

2.2 Idiopathic Pulmonary Fibrosis (IPF)

The symptoms of IPF are breathlessness, cough, and fatigue (Shaw et al. 2017). It affects more than 32,000 people in the UK or 1 in 2000 people. About 1 patient has IPF for every 30 patients with COPD. Worldwide the prevalence of IPF is 2.8–9.3 per 100,000 (Hutchinson et al. 2015). Each GP is likely to have a little less than one patient with IPF on his or her list in the UK at any one time. There are 5000 deaths from IPF in the UK each year (Navaratnam et al. 2011). On average a primary care team will have a patient who dies from IPF every 2–3 years. This is about a sixth of the deaths that might be expected from COPD.

In IPF, the diagnosis and severity are defined by the spirometric criterion of forced expiratory volume (FEV). The treatment of IPF has changed in the last 5 years with the publication of two trials of antifibrotic drugs. These two drugs, pirfenidone and nintedanib, have been shown to reduce the progression of the disease (NICE 2016; Nathan et al. 2017). It is not yet clear how well this treatment will control the impact of IPF. If successful it will significantly reduce the burden of IPF at the end of life.

2.3 Cystic Fibrosis

About 10,000 people in the UK have cystic fibrosis, the commonest inherited disease affecting Caucasians. It is a common reason for lung transplant. Dramatic changes have occurred in the life expectancy of CF (Keogh et al. 2018). At birth people with CF should now expect to live until their mid-40s. People with CF at 30 years should expect to live into their mid-50s. In 10 years life expectancy is projected to be in the mid-60s for people aged 30. Better understanding of the underlying mechanisms is likely to lead to significant improvements in the treatment of cystic fibrosis. For now, the most important intervention is early treatment of respiratory infections with the prevention of mucous plugging if possible. Respiratory failure is the commonest cause of death. It is difficult to define the burden of cystic fibrosis on palliative care services because deaths are sporadic, result from acute infections, or occur in people in lung transplant programs.

3 The Symptoms

In advanced respiratory disease, four symptoms dominate patients' experience: breathlessness, cough, weakness, and low mood.

Breathlessness is the central problem in loss of respiratory function, the chief impact of these diseases. In COPD breathlessness progresses gradually. Sometimes it deteriorates so slowly that it is the loss of functional capacity that makes the change apparent. Breathlessness is difficult to remedy. There is a variety of strategies that can ameliorate its impact in people with advanced disease, including exercise to improve muscular fitness, breath training to give greater control of the symptom, psychological strategies to reduce the anxiety that often accompanies the symptom, mechanical devices to distract from the symptom, and pharmacological interventions to reduce its perception. These are discussed in more detail later in the chapter.

Cough is usually a more prominent symptom in early disease. However, in IPF cough progresses with the disease, and 80% of patients with advanced IPF have cough (Shaw et al. 2017). In IPF the symptom is often intractable, and treatment is usually ineffective. In COPD cough is usually productive. It can become intractable in advanced disease especially when associated with difficulty in clearing secretions from the upper airway. There has been more interest in recent years in the use of mucolytics such as carbocysteine, but evidence for their effectiveness is moderate.

Weakness is the culmination of the downward spiral that results from progressive breathlessness. Breathlessness leads to reduced exercise that in turn leads to muscle deconditioning. With muscle deconditioning, there is less efficient use of oxygen so that more breathing is required to achieve the same functional result and the outcome is weakness. In advanced disease, exhaustion and demoralization can follow minor physical activity. In COPD, in IPF, or in CF, there is no evidence of inflammatory activity outside the respiratory system. The progressive weakness that occurs is not due to peripheral myopathy or neuropathy.

The most effective treatment of the progressive symptoms and disability of COPD and IPF, and possibly CF, is pulmonary rehabilitation, which converts the downward spiral of progressive weakness into a virtuous cycle (McCarthy et al. 2015). It improves breathlessness, exercise capacity, sense of mastery over the disease, and anxiety. Pulmonary rehabilitation is a treatment based on exercise, disease education, and social interaction. Participants usually attend between 8 and 12 classes spread over 6–10 weeks. The main effect of pulmonary rehabilitation is improved exercise capacity in the muscles, but there is now increased evidence, from brain scanning, that pulmonary rehabilitation is also associated with changes in the neural responses in the brain to breathlessness, which alter the perception of breathlessness (Herigstad et al. 2017). The challenge for clinicians in treating patients with advanced disease is to judge whether their patients can undertake pulmonary rehabilitation. Evidence for the effectiveness of pulmonary rehabilitation in moderate and severe disease is undisputed. There has been less study of its effect in patients with advanced disease, but such is its effectiveness in other groups; it should be considered in the most severely affected patients.

Low mood together with anxiety is a common accompaniment of chronic breathlessness and is frequently seen in COPD and IPF. The evidence for the effectiveness of the treatment of psychological symptoms in moderate or severe respiratory disease is limited. Chronic breathlessness often leads to social isolation and dependence on carers. The progressive deterioration seen in COPD, in IPF, and in cystic fibrosis is dispiriting. The chronic breathlessness also leads to insomnia and loss of established sleep patterns. In COPD, commonly caused by smoking, many patients will have suffered criticism from family, friends, and health professionals for failing to give up smoking. The implication of this criticism is that the disease has been self-inflicted, and some patients with advanced COPD feel undeserving of treatment or of the support of family and friends.

IPF by contrast with COPD is of unknown cause, has no specific treatment, and will be completely unfamiliar to most patients. IPF and CF patients may not share the sense of blame that is common in COPD. They are more likely to feel perplexed and hopeless. For all of these patients, the burden of the disease is immense, and patients' resilience is undermined further by low mood and anxiety.

4 Trajectory and Prognosis in Advanced Progressive Respiratory Disease

Prognosis is one of the more vexed areas in the management of advanced chronic respiratory disease. With IPF prognosis is worse than in many cancers. As respiratory function deteriorates, it is possible to predict roughly when a patient is likely to die (Shaw et al. 2017). The advantages that accompany this relative accuracy are the opportunities for informing patients and their families what is likely to lay ahead and for enabling patients and families to plan for the implications of the patient's death.

In cystic fibrosis prognosis is a much less precise possibility. While the disease is progressive, deterioration is determined by respiratory infection (Keogh et al. 2018). Damage is caused to the lung parenchyma by infection and mucous plugging. With each infection the process is accelerated. This is a well-documented trajectory. Death is unpredictable because it is likely to occur during an infection. The gaps between infections may be prolonged. However, the experience of people dying very prematurely from cystic fibrosis has

led to little attention to the palliative care aspects of the disorder in the research literature. Recent research on palliative care of CF has suggested that the preoccupation with preventing further progression of the disease may have drawn attention from the need to prepare those for whom death was a likely possibility. Patients and families may be unprepared for deterioration and death.

The situation with COPD is strikingly different. For many years it was the hope of most people interested in improving the management of advanced chronic respiratory disease that with more careful assessment and more careful research, it would be possible to make the prediction of the risk of death more accurate. Alas we are now more confident than ever that there is little hope of predicting the risk of death within a year in COPD.

5 Issues in Specific Diseases

5.1 COPD

The clarity with which patients with advanced COPD have indicated breathlessness as their dominant symptom, while affirming their commitment to living presents a complex dilemma (White et al. 2011; Pinnock et al. 2011). Breathlessness is a very difficult symptom for which there are limited therapeutic options. Yet patients would prefer to take their chances with the next exacerbation, with the limited treatment available, than hope for their symptoms to be relieved by death. The severity of breathlessness in COPD has been compared with that in advanced cancer (Gore et al. 2000). How is it that COPD patients with breathlessness in advanced disease manage their everyday lives? Clearly it is not easy, but a number of factors distinguish patients with COPD from those with cancer and indeed patients with IPF. The breathlessness of COPD is slow in developing, often over more than 20 years. As it progresses it is likely that patients adjust to the symptom in their perception and in their expectations. If the status quo is breathlessness on exertion, then the symptom will have no surprise element, and impaired function will the norm. As breathlessness at rest increases then, there are the accompanying problems of exhaustion, low mood, and progressive immobility. But COPD patients are often remarkably phlegmatic and accept these changes as part of the disease.

Prognosis in COPD is a thorny issue. In a landmark study in the USA in 1996, of 1016 COPD patients admitted with Type II respiratory failure (hypercapnia ± hypoxia), 50% were still alive after 2 years (Connors et al. 1996). Six years later this study was effectively repeated on a smaller scale in Spain (Almagro et al. 2002). In the later study, the survival in a similar group of patients was 65%. In such severely affected patients, the most accurate prognosis possible was a risk of dying between 35% and 50% within 2 years.

Some 15 years ago, COPD patients were reported to have expressed an interest in knowing their prognosis when asked if they wanted their physician to discuss it with them (Curtis et al. 2004). There are concerns as to whether it is ethical to ask research participants this question when an accurate prognosis was beyond the capacity of specialists or generalists. A conclusion to this question has been effectively drawn by the latest work by Almagro and colleagues (2017). They have demonstrated that a prognosis of less than 1 year is impossible to make in advanced COPD with all the disease-specific and general demographic information available.

For patients with advanced COPD or CF, and their clinicians, introducing the subject of advance care planning may seem counter to the flow of communication. One of these exacerbations may be fatal. Has important communication of this risk been considered with dependents and key intimates in their lives? Do affairs need to be put in order? Are there treatment options that should be reviewed? This opportunity must be seized because it is unlikely that a definitive prognostic moment will present itself. The opportunity is the result of increasing risk in a long trajectory of risk.

The supportive care of advanced COPD and of CF should include discussion of the stage of the disease, the likely progression of symptoms, the potential complications, and the available treatments. Progression may be accelerated by

exacerbations. The role of smoking cessation in advanced disease is uncertain. More than 40% of people with moderate, severe, or very severe disease, in whom smoking was the main cause of the disease, continue to smoke.

Since survival is important to people with advanced COPD, how can end-stage disease be identified? The terminal stage of COPD, the stage of imminent death, can be identified by a combination of conventional or generic signs of diminishing functional capacity. These include requirement of help with eating, drinking, washing, and toileting by becoming bedbound, by loss of appetite, and by severe weight loss or cachexia. In the presence of advanced COPD, with no other explanation, these signs are suggestive of imminent death. Such a case is presented in Box 1.

Box 1 A Story of Imminent Death in COPD

MD, a single man of 57 years, had COPD diagnosed at the age of 54. His COPD probably began in his mid-40s to judge from the onset of his cough and breathlessness. He was a scaffolder until 2 years ago, when his breathlessness stopped him from working. He had two hospital admissions due to his COPD in the previous 6 months. The most recent was associated with a marked deterioration. He had been ventilated during the admission and was in the hospital for nearly 3 months. No other cause was found. The doctors said there was nothing more that could be done, and he was at risk of readmission. On discharge from the hospital, he was breathless at rest and prone to confusion. He was on long-term oxygen therapy for chronic hypoxia. He was taking his inhaled drugs by nebulizer every 4 h.

He was looked after at home by his two sisters, one of whom had come to stay. Within 2 weeks of his discharge, he had deteriorated again. He was more short of breath and confused, and he was refusing food. With his sisters' help, he was using a commode. At this point his GP, who had known him for years, was shocked at his cachectic state. He wanted to readmit him to the hospital. His sisters pleaded for him not to be readmitted because he had asked them to promise not to let him be sent back. They felt that he was dying.

The GP examined him. MD was confused. His heart rate was 104/min; his respiratory rate was 36/min. He was cyanosed. There was no fever and no evidence of pneumonia. After discussion with MD's sisters, it was agreed that MD would spend the night at home and that an urgent request for assessment by the palliative care team would be made. The GP told the sisters that MD may not survive for many days in this condition. They said they knew that already.

The following day a call came from MD's sisters. He had died during the night.

The uncertain trajectory of advanced COPD, the prolonged experience of severe symptoms, and the long-term adjustments that patients make demand a palliative care approach which is about support, symptom management, and psychological adjustment. End-of-life care is not the dominant concern in COPD for the main part. Patients with advanced COPD are more likely to see themselves living with their disease than dying from it. Until they enter that final period in which cachexia and rapid loss of function are the predominant features, it is more appropriate to provide palliative care that has an outlook that matches that of the patient. Interventions should be symptom-responsive. Talk about symptom management and supportive care should be the dominant component where appropriate, not preparation for the imminent end to life.

5.2 Idiopathic Pulmonary Fibrosis

IPF presents an altogether different challenge to that of COPD. It is a disease with a limited prognosis from the outset. The annual rate of

decline of FEV_1 from diagnosis is usually between 10% and 20% of expected so that the progression of the symptoms is so rapid that there is much less time for adjustment than is seen in COPD. The loss of function is more obvious and more alarming to family and friends. The diagnosis is like that of a malignant disease, with moderate but relentless progression. As the disease progresses, so does functional impairment. The value of pulmonary rehabilitation at this stage should not be underestimated. It is common for the suggestion of the potential benefits of pulmonary rehabilitation to be lost on breathless patients. Recovering a small degree of functional improvement can make a surprising difference.

Early and effective information provision in IPF for the patient and for carers can allow for effective planning. Advance planning is needed to prepare for inevitable challenges at work, for financial commitments, for discussion with close family, and for the preparation of impending loss. Patients with IPF should be considered early for referral to multidisciplinary clinics for the management of breathlessness. The rapid deterioration in symptoms may mean that there is a greater role for psychological interventions for breathlessness and for the use of opioids.

The recent introduction of antifibrotic drugs, pirfenidone, and nintedanib, for IPF, has been shown to slow the progression of the disease in many patients (Nathan et al. 2017; NICE 2016). Should this intervention be shown to be effective in the later stages of the disease, there may be hope that its terminal stages can be postponed.

While the rate of deterioration in IPF is rapid by comparison to COPD, it is an uncommon disease, and little research has been done on the palliative care of the condition. Careful monitoring of change in FVC can be used, and from this the clinician can obtain a relatively accurate estimate of prognosis.

5.3 Cystic Fibrosis

Change in the last 50 years in the life expectancy of cystic fibrosis from birth has been remarkable. The progress of cystic fibrosis is usually intermittent, but 50 years ago the prognosis from birth was less than 15 years. Even before the disease becomes advanced, the life-threatening nature of acute infections may be unavoidable. Acute severe infections should provide a timely opportunity to consider how interventions can be optimized and the importance of early intervention with antibiotics in worsening breathlessness. They also show how such infections raise problems of antimicrobial resistance and the risk of dying. Advance care planning in CF requires good continuity of care especially as sufferers move through adolescence.

Little research has been published on the palliative care of CF. It seems likely that the patient, the carers, and the clinicians become preoccupied with early intervention and careful management of acute exacerbations of the disease. At some point there must be an opportunity to consider the increasing risk that the patient faces of an exacerbation being life-threatening. This may be addressed when patients are considered for lung transplant. There will have been appropriate and earlier occasions when the subject could have been raised. It would be remiss of services not to respond to the opportunity at the right time.

6 The Assessment and Treatment of Breathlessness

Breathlessness in advanced disease has a variable association with measures of respiratory function, particularly reductions in FEV_1 and FVC. The control of breathing and the experience of breathlessness are determined by a complex array of physiological and psychological influences and controls (Currow et al. 2016). These include the peripheral stimuli associated with movement in the muscles of respiration; the movement of air in the face, mouth, and pharynx; and drying of the mouth and pharynx with increased breathing. Internal factors include levels of oxygen, carbon dioxide and acid/base balance in the blood, and emotional factors, including expectations and learned responses. Such is the complexity of the

interactions of these different elements that it is hardly surprising that people have very different experiences of breathlessness for the same levels of disease severity. To understand the role of treatments for breathlessness in advanced disease, it is worth considering the underlying issues of low oxygen (hypoxia) and raised carbon dioxide (hypercapnia) in advanced respiratory disease.

The effect of impaired breathing due to obstruction and parenchymal damage in COPD, and due to restriction of respiratory movement in IPF, is to reduce the delivery of oxygen (O_2) into the blood and to reduce the removal of carbon dioxide (CO_2). Patients with advanced COPD usually develop tolerance in the brain to increased CO_2 (hypercapnia). The main drive to breathing in established COPD is reduced oxygen in the blood, hypoxia. In such patients complete relief of hypoxia by giving O_2 diminishes the drive to breathe. If the drive to breathe is reduced, the CO_2 level in the blood may rise to dangerous levels. This can cause the patient to become drowsy or unconscious – CO_2 narcosis – and ultimately to be in danger of dying. Patients dependent on hypoxia for the drive to breathe may be at considerable risk in receiving unlimited O_2 for symptom relief.

On the other hand, patients with persistent hypoxia may require long-term oxygen therapy to prevent pulmonary hypertension. The identification of hypoxia, O_2, below a saturation of 92% on a pulse oximeter, should lead to specialist referral for consideration of long-term oxygen therapy.

For patients that become intermittently hypoxic on exercise, intermittent oxygen may be needed. In the unusual situation that a severely ill patient becomes hypoxic at rest, then low dose (2 L/min) oxygen can be administered to relieve breathlessness until the patient is assessed by a specialist. The relief obtained is likely to be small if any.

The perception of breathlessness in the brain is complex. It varies from person to person, some people appearing to tolerate breathlessness in more severe disease than others. Breathlessness perception and the tolerance of breathlessness can be markedly affected by anxiety. Understanding the mechanisms of breathlessness is tied to the therapies that are brought to bear on the symptom in advanced disease. These are pulmonary rehabilitation, breathing training and exercises, therapy for anxiety, handheld fan, neuromuscular electrical stimulation, and the suppression of the perception of breathlessness with drugs (Higginson et al. 2014; Farquhar et al. 2016; Maddocks et al. 2017). Pulmonary rehabilitation and a handheld fan can be prescribed in primary care. If the patient needs breathing training, therapy for anxiety, neuromuscular electrical stimulation, or the use of drugs, referral should be made to a multidisciplinary center.

Breathing training and exercises work by promoting more efficient posture for breathing and by reinforcing the sense of control of breathing when the patient is more breathless through specific physical strategies to manage the breathlessness. Some people experience a cycle of worsening breathlessness in which the breathlessness causes anxiety, which in turn leads to hyperventilation and a sensation of even worse breathlessness. This combination is difficult to identify. It may be evident from an exceptional response to breathing exercise which is accompanied by a marked reduction in anxiety. The handheld fan is of variable value. It probably works by blowing air across the lips and cheeks generating a sense of greater movement of air and of more effective breathing. Neuromuscular electrical stimulation is designed to improve breathlessness by improving peripheral muscle power (Maddocks et al. 2016). It is effective in reducing the effect of exercise on breathlessness. But how long the effect is sustained has not been assessed, and it is only available in specialist centers.

The suppression of breathlessness by opioids has been used for many years in people with advanced cancer, particularly in their last days. The development of tolerance and dependence is not an issue in such circumstances. In advanced respiratory disease, the circumstances are different. Evidence is slowly coming to light about appropriate dosing and the risks of prolonged use. The case in Box 2 highlights some of the issues.

Box 2 Opioids in Chronic Respiratory Breathlessness? A Case History

SB, a widower of 74 years, had COPD for 15 years. Having been a smoker since a teenager, he was still smoking three or four cigarettes a day. He lived alone and was a volunteer driver for the local hospital, taking patients to and from their appointments. He liked his voluntary work, but his breathlessness was increasingly troublesome. He had difficulty sleeping at night and had to sit up. He was on maximal treatment for his COPD. He was not hypoxic. His GP referred him to the local chest clinic to rule out lung cancer.

The chest physician investigated SB. No new problems were identified. There was no sign of cardiac disease. He was told to continue on his medications and discharged from the clinic. He had started pulmonary rehabilitation 6 months ago, but he did not think it was helping, so he stopped after two sessions.

After another 6 months, SB's breathlessness was worse. He now spent all of his time at home, breathless at rest. He was again referred to the chest physician who discharged him saying there was no further treatment that would help his COPD.

SB's GP did not know what to do next. She referred SB to the local palliative care breathlessness clinic. SB was seen there by a palliative care physician and palliative care nurse.

SB was referred to a psychologist to treat the anxiety associated with his breathing and to a physiotherapist for breathing exercises and breathing training. He was given a handheld fan. After 4 months there was little change. SB was then started on oral morphine 2.5 mg four times daily. His breathing improved for the first time in perhaps a year. His exercise capacity was no different, but he felt better and slept better. SB was admitted to the hospital with an exacerbation of COPD 9 months after starting morphine. He was taking 5 mg in the morning and the evening and 2.5 mg twice during the day. His breathlessness was still better. Sadly he developed pneumonia and died.

It is clear that this patient has advanced COPD. The multidisciplinary team had run out of options, and so morphine was started. He was taking relatively small amounts of morphine for a prolonged period of 9 months until an exacerbation led to his death. It is unclear if the morphine retained its effectiveness or whether the increase in dosing had an impact on his death in terms of his response to the exacerbation. The morphine had been very helpful in improving the symptom for a long period of time.

The usual dosage of morphine currently recommended for advanced respiratory disease is a starting dose of 10 mg daily as a sustained release preparation (Smallwood et al. 2015). This can also be administered as 2.5 mg of immediate acting morphine up to four times daily. The maximum dose should be 30 mg. There is no evidence of difference of effectiveness between different opioids, but most of the current evidence relates to morphine. Among the issues yet to be addressed with respect to morphine use in advanced respiratory disease are the long-term effects on survival, the development of tolerance, the sustained effect on symptoms, and the need for larger amounts during exacerbations. Within the dosage guidance described here, general practitioners may wish to start opioids for COPD patients with intractable. It may be wise to do so with the support of a palliative care team for those who are inexperienced. It should only be initiated for advanced respiratory disease in specialist centers until evidence for its use becomes clearer.

7 Supporting Carers in Respiratory Disease

Carers of people with advanced IPF have needs that are similar to those of carers with advanced cancer. The needs of carers of people with COPD

and CF are different. It is only recently that the needs of this group have begun to be examined (Farquhar 2017). They relate to the slow progression of the disease, the lack of certainty about the prognosis, the frequency of exacerbations, and the isolation that comes with caring for a person with severe functional impairment who may be housebound. Spouses or partners do much of the caring. Just as many people with COPD have comorbidities, so do many of their carers.

8 Conclusion

The goal of treatment of advanced progressive respiratory disease must be in keeping with both the aspiration of patients and the practical realities of the stage of the disease. In COPD and in CF, defining prognosis is so difficult that priority should be given to informing patients and trying to meet their hopes and expectations. In IPF, prognosis may be so limited that clear information about the risk of impending death should be available to the patient and the relatives in line with their perceived need. In COPD and in CF, breathlessness may become slowly intractable over 20 or more years so that life eventually becomes barely tolerable. In IPF this is likely to be the case at a more rapid pace over 2–3 years. There are many remedies to be considered in the breathlessness of COPD and IPF. In all three diseases, morphine may have a role in reducing the perception of breathlessness. In IPF morphine may also have a role in cough which affects 80% of sufferers and is progressive. Morphine in low doses does not suppress breathing, does not appear to generate tolerance, and seems safe in the breathlessness of advanced respiratory disease.

References

Almagro PL, Calbo E, Ochoa de Echagüen A, Barreiro B, Quintana S, Heredia JL, Garau J. Mortality after hospitalization for COPD. Chest. 2002;121(5):1441–8.

Almagro P, Yun S, Sangil A, Rodríguez-Carballeira M, Marine M, Landete P, Soler-Cataluña JJ, Soriano JB, Miravitlles M. Palliative care and prognosis in COPD: a systematic review with a validation cohort. Int J Chron Obstruct Pulmon Dis. 2017;12:1721–9. https://doi.org/10.2147/COPD.S135657. eCollection 2017.

British Lung Foundation. Chronic obstructive lung disease statistics [online]. 2018. Available at https://statistics.blf.org.uk/copd. Accessed 2 Jan 2018.

Connors AF Jr, Dawson NV, Thomas C, Harrell FE Jr, Desbiens N, Fulkerson WJ, et al. Outcomes following acute exacerbation of severe chronic obstructive lung disease. The SUPPORT investigators (Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments). Am J Respir Crit Care Med. 1996;154(4 Pt 1):959–67.

Currow DC, Abernethy AP, Allcroft P, Banzett RB, Bausewein C, Booth S, et al. The need to research refractory breathlessness. Eur Respir J. 2016;47(1):342–3.

Curtis JR, Engelberg EL, Nielsen DH, Patrick DL. Patient-physician communication about en-of-life for patients with severe COPD. Eur Respir J. 2004;24:200–205. https://doi.org/10.1183/09031936.04.00010104.

Farquhar M. Assessing carer needs in chronic obstructive pulmonary disease. Chron Respir Dis. 2017. https://doi.org/10.1177/1479972317719086.

Farquhar MC, Prevost AT, McCrone P, Brafman-Price B, Bentley A, Higginson IJ, Todd CJ, Booth S. The clinical and cost effectiveness of a Breathlessness Intervention Service for patients with advanced non-malignant disease and their informal carers: mixed findings of a mixed method randomised controlled trial. Trials. 2016;17:185. https://doi.org/10.1186/s13063-016-1304-6.

Gore JM, Brophy CJ, Greenstone MA. How well do we care for patients with end stage chronic obstructive pulmonary disease (COPD)? A comparison of palliative care and quality of life in COPD and lung cancer. Thorax. 2000;55(12):1000–6.

Herigstad M, Faull OK, Hayen A, Evans E, Hardinge FM, Wiech K, et al. Treating breathlessness via the brain: changes in brain activity over a course of pulmonary rehabilitation. Eur Respir J. 2017;50(3):1701029. https://doi.org/10.1183/13993003.01029-2017

Higginson IJ, Bausewein C, Reilly CC, Gao W, Gysels M, Dzingina M, et al. An integrated palliative and respiratory care service for patients with advanced disease and refractory breathlessness: a randomised controlled trial. Lancet Respir Med. 2014;2(12):979–87.

Hutchinson J, Fogarty A, Hubbard R, et al. Global incidence and mortality of idiopathic pulmonary fibrosis: a systematic review. Eur Respir J. 2015;46:795–806.

Keogh RH, Szczesniak R, Taylor-Robinson D, Bilton D. Up-to-date and projected estimates of survival for people with cystic fibrosis using baseline characteristics: a longitudinal study using UK patient registry data. J Cyst Fibros. 2018. https://doi.org/10.1016/j.jcf.2017.11.019. pii: S1569-1993(17)30976-1. [Epub ahead of print].

Maddocks M, Nolan CM, Man WD, Polkey MI, Hart N, Gao W, et al. Neuromuscular electrical stimulation to improve exercise capacity in patients with severe

COPD: a randomised double-blind, placebo-controlled trial. Lancet Respir Med. 2016;4(1):27–36.

Maddocks M, Lovell N, Booth S, Man WD, Higginson IJ. Palliative care and management of troublesome symptoms for people with chronic obstructive pulmonary disease. Lancet. 2017;390(10098):988–1002.

McCarthy B, Casey D, Devane D, Murphy K, Murphy E, Lacasse Y. Pulmonary rehabilitation for chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2015;(2):CD003793. https://doi.org/10.1002/14651858.CD003793.pub3. Review.

Nathan SD, Albera C, Bradford WZ, et al. Effect of pirfenidone on mortality: pooled analyses and meta-analyses of clinical trials in idiopathic pulmonary fibrosis. Lancet Respir Med. 2017;5:33–41.

Navaratnam V, Fleming KM, West J, et al. The rising incidence of idiopathic pulmonary fibrosis in the UK. Thorax. 2011;66:462–7.

NICE (National Institute for Health and Care Excellence). Nintedanib for treating idiopathic pulmonary fibrosis (TA379). London: NICE; 2016.

Pinnock H, Kendall M, Murray SA, Worth A, Levack P, Porter M, et al. Living and dying with severe chronic obstructive pulmonary disease: multi-perspective longitudinal qualitative study. BMJ. 2011;342:d142. https://doi.org/10.1136/bmj.d142.:d142.

Shaw J, Marshall T, Morris H, Hayton C, Chaudhuri N. Idiopathic pulmonary fibrosis: a holistic approach to disease management in the antifibrotic age. J Thorac Dis. 2017;9(11):4700–7. https://doi.org/10.21037/jtd.2017.10.111.

Smallwood N, Le B, Currow D, Irving L, Philip J. Management of refractory breathlessness with morphine in patients with chronic obstructive pulmonary disease. Intern Med J. 2015;45(9):898–904. https://doi.org/10.1111/imj.12857.

White P, White S, Edmonds P, Gysels M, Moxham J, Seed P, Shipman C. Palliative care or end of life care in advanced COPD? A prospective community survey. Br J Gen Pract. 2011. https://doi.org/10.3399/bjgp11X578043.

White P, Thornton H, Pinnock H, Georgopoulou S, Booth H. Overtreatment of COPD with inhaled corticosteroids – implications for safety and costs: cross-observational study. PLoS One. 2013;8(10):e75221. https://doi.org/10.1371/journal.pone.0075221.