

Chronic obstructive pulmonary disease: reasons for optimism

Chronic obstructive pulmonary disease (COPD) is a growing global epidemic that is now a leading cause of mortality, and the only common cause of death that is increasing [1]. It is also a common and increasing cause of morbidity, with progressive worsening of quality of life. COPD is a highly prevalent disease, and population studies show that it now affects 5–10% of the population over 40 years, although there are wide variations in prevalence between countries [2]. Most individuals with COPD are undiagnosed and therefore untreated, and this is especially true for women. Surprisingly, COPD is now just as prevalent in females as in males in developed countries, and the issue of gender and COPD is discussed in detail by de Torres and colleagues in this issue [3]. It is predicted that morbidity and mortality will continue to rise as populations age and mortality from cardiovascular and infectious diseases falls, particularly in developing countries. While cigarette smoking is the most common cause of COPD in developed countries, it is now clear that COPD is also seen in nonsmokers, and that this is particularly true for developing countries, yet very little is known about this nonsmoking form [4]. COPD is primarily characterized by the presence of airflow limitation resulting from inflammation and remodeling of small airways, and is often associated with lung parenchymal destruction or emphysema. It is increasingly recognized that COPD extends beyond the lung and that many patients have several systemic manifestations that can further impair functional capacity and health-related quality of life [5]. In addition, COPD is associated with several other diseases, such as cardiovascular diseases, osteoporosis, diabetes and metabolic syndrome, more commonly than expected by chance, and common etiological factors such as smoking suggest that these co-morbidities are causally associated. Systemic effects and co-morbidities increase the risk of hospitalization, mortality and the costs of COPD, and are therefore a topic of increasing concern [6]. The recognition that COPD is a disease of major and increasing importance worldwide has now created considerable interest amongst respiratory specialists and in general practice where most of the disease is managed. There is now

increased understanding of the underlying cellular and molecular mechanisms, which is beginning to identify novel targets for therapy [7]. The pharmaceutical industry has now recognized that COPD is a common disease with a global dimension, which represents the greatest unmet need of any disease known. COPD patients suffer exacerbations that makes it one of the most common causes of hospital admission in many countries [8]. The high prevalence, repeated hospital admissions and loss of time from work from COPD impose a high and increasing economic burden, which is now causing considerable concern to governments. This has resulted in an enormous surge in clinical and basic research on COPD. This issue of *Therapy* focuses on some of the novel and emerging aspects of this important disease.

It is now clear that COPD, which is defined by poorly reversible airflow limitation, includes several different diseases or subphenotypes and these are discussed by Polverino and Cosio [9]. It is important to discover whether different subphenotypes have differing natural histories, co-morbidities and response to therapy, particularly as new drugs are tested. The use of biomarkers, such as inflammatory mediators and proteases, may facilitate the recognition of subphenotypes in the future, and this may be supplemented by genomic and proteomic analyses and the use of systems biology to recognize different subphenotypes. Perhaps we may even end up with many 'orphan' diseases within the umbrella of COPD [10].

It is now increasingly recognized that COPD has a major impact on the wellbeing of patients, which increases as the disease progresses, and that this includes cognitive defects. Hung and Wisnivesky highlight the importance of cognitive defects, particularly in patients with severe COPD, and suggest that cognitive screening may be useful as these defects are often overlooked [11,12]. Recognition of cognitive dysfunction is important as it may affect self management and adherence to therapy. Many co-morbidities are now associated with COPD, and their presence has an important impact on prognosis and therapy. One of the most common co-morbidities is lung cancer, which is a common cause of death in COPD patients, particularly those with severe



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disease and with emphysema. The much greater prevalence of lung cancer in COPD patients compared with smokers who do not have airflow limitation is almost certainly linked to chronic inflammation in the respiratory tract, as discussed by Gibbons and Sethi in this issue [13]. The molecular pathways involved in this increased cancer risk are now being dissected, and this knowledge may lead to more effective treatment for COPD and lung cancer in the future.

Pharmacological therapy for COPD has greatly improved over the last few years, and nonpharmacological treatments, such as pulmonary rehabilitation, are now recognized as very important components of COPD management [14]. Wouters and Vanderhoven-Augustin emphasize the importance of moving away from a crisis-driven therapeutic approach to patient-centered integrated care, with recognition of the complexity of this disease and its co-morbidities and the need for long-term management strategies [15].

New therapies are urgently needed for COPD, yet there have been no new classes of drug introduced for the treatment of COPD over the last 30 years. There have been important improvements in bronchodilator therapy, which have brought major clinical benefits to patients, with reduced symptoms, improved health status, reduced numbers of exacerbations and possibly reduced mortality, but there are currently no effective anti-inflammatory therapies on the market. However, several novel drugs are now in development for COPD, as emphasized by Rennard in his interview [16] and summarized by Barnes [17]. The

most advanced of these new therapies are phosphodiesterase-4 inhibitors and the oral drug roflumilast provides small but consistent clinical benefit [18]. In addition to novel drugs, mesenchymal stem cells may provide a way of repairing damaged lung and even reversing COPD in the future. As Groves and colleagues point out, there are encouraging results of using mesenchymal stem cells in animal models of COPD [19], and a pilot study in COPD patients indicates some potential for these stem cells in reducing inflammation.

There are now reasons for optimism about COPD, with greater recognition of the disease, major improvements in management and the prospects of several new therapies that might be applied early in the disease to prevent its progression. There is no doubt that the new investment in COPD research will bring increasing clinical benefits to our patients who suffer from this terrible disease.

Financial & competing interests disclosure

Dr Barnes has served on Scientific Advisory Boards of AstraZeneca, Boehringer-Ingelheim, Chiesi, GlaxoSmithKline, Novartis, Pfizer, Teva and UCB and has received research funding from AstraZeneca, Boehringer-Ingelheim, Chiesi, Daiichi-Sankyo, GlaxoSmithKline, Mitsubishi-Tanabe, Novartis and Pfizer. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

No writing assistance was utilized in the production of this manuscript.

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