

Cystic fibrosis (CF), an autosomal recessive genetic disorder, is a multisystem disease in the course of which pulmonary infection and inflammation cause the greatest morbidity and mortality. The respiratory therapist (RT) and others caring for patients with respiratory disease are intimately involved in the care of patients with CF. In the May and June 2009 issues of RESPIRATORY CARE, we are pleased to present the papers from the 43rd RESPIRATORY CARE Journal Conference, which provides a state-of-the-art review of current knowledge of CF pulmonary disease and respiratory care. Internationally recognized experts in the science of CF and the care of persons with this disease gathered to review the pulmonary pathophysiology of CF. The papers from this conference are a must-read for the RT and anyone else involved in the care of patients with CF. We are grateful to Bruce Rubin and David Geller for their hard work in organizing this conference and for helping to edit the proceedings.

Although much of the care of patients with CF occurs in specialized referral centers, most RTs and other respiratory clinicians will see patients with CF at one time or another in their careers. Once considered a disease of children, patients with CF are increasingly living to adulthood. RTs are involved in the care of these patients through teaching and applying airway clearance techniques, administering therapeutic aerosols, performing pulmonary function testing, and caring for patients requiring invasive and noninvasive ventilation. Research RTs are at the forefront of new discoveries and the application of new therapies. As Volsko points out, the role of the RT in the care of patients with CF has expanded throughout the years. RTs are key members of the multidisciplinary team caring for these patients, in both the acute in-patient and chronic out-patient settings.

Ratjen shows how CF can serve as a paradigm of how a better understanding of the underlying disease process can translate into new and potentially more causative treatment approaches. Since the detection of the underlying gene defect in 1989, our knowledge of how the genetic mutations in CF cause lung disease has increased substantially, leading to new therapeutic approaches that address key factors of CF pathophysiology. Past therapeutic successes were largely based on targeting the *consequences* of the CF transmembrane regulator dysfunction, such as phlegm retention, infection, and inflammation. These are important, but, as Ratjen states, new therapies may be able to address the *underlying abnormality* rather than the downstream effects. The future prospects of these therapies are exciting and may affect treatment in a profound way. One of the most exciting of these therapies is the potential for gene replacement therapy. Treating the early and root causes of CF will improve not only patient outcomes, but may also reduce the substantial burdens of treatment for the patient and the patient's family.

As is the case with any chronic disease, it is important to monitor respiratory disease severity in CF. As suggested by Davies and Alton, measurements of disease severity provide a guide for the clinician to tailor therapies and for the patient and family to gauge progress. Such monitoring is particularly important in clinical trials. For many respiratory diseases, including CF, there are few sensitive, noninvasive measurements. Unfortunately, those that are available lack sufficient sensitivity or are applicable only to certain subgroups of patients. The authors discuss the strengths and weaknesses of a number of measurements, including spirometry, plethysmography, lung-clearance index, sputum and bronchoalveolar lavage evaluations, exhaled nitric oxide, exhaled breath condensate, radiology, and others.

There is no debate that earlier diagnosis, treatment of exacerbations, and the use of long-term therapies have improved the lifespan of patients with CF. However, as Flume explains, the progression of airways disease leads to respiratory failure. Moreover, some patients will experience other acute respiratory complications such as pneumothorax and massive hemoptysis. Without question, RTs and others caring for these patients should be aware of the implications of these complications. Aggressive treatment including airway-clearance therapies of the underlying condition is imperative.

Some clinicians have argued that airway-clearance therapies might aggravate or precipitate complications. However, airway-clearance therapies can probably be performed safely. Knowledge of alternative therapies that are effective but may place the patient at less risk is important. Inhaled dornase alfa and tobramycin have been associated with a lower incidence of massive hemoptysis and are recommended therapies for patients with advanced airways disease. But, they are also associated with a higher incidence of pneumothorax. This suggests careful assessment of the potential for these drugs to induce bronchospasm in these patients. It is prudent to use spirometry to evaluate the acute effects of inhaled medications on airway reactivity. As Flume cautions, clinicians should be cognizant of the potential pulmonary complications that result from the chronic infection and inflammation of CF, most notably pneumothorax, hemoptysis, and eventual respiratory failure.

As stated by Davies and Bilton, bacteria infect the respiratory tract early in the course of CF, often fail to be eradicated, and, together with an aggressive host inflammatory response, are thought to be key players in the irreversible airway damage from which most patients ultimately die. *Staphylococcus aureus*, *Haemophilus influenzae*, and *Pseudomonas aeruginosa* are common CF pathogens, but several newer species are becoming more common. Aspects of airways in patients with CF appear to favor the development of chronic modes of survival of bacteria. Formation of biofilm is particularly important, which makes bacteria more resistant to antibiotics. The development of antibiotic resistance is also of concern. Of course, the best therapy is prevention, which can be aided by infection-control measures. Of particular interest in this paper is the discussion of the 8 basic tenets of antibiotic treatment for patients with CF.

O'Malley addresses issues of infection control in CF, particularly the important issues of cohorting and cross-contamination. Increasing evidence of patient-to-patient transmission of CF pathogens led the Cystic Fibrosis Foundation (CFF) to produce evidence-based infection-control recommendations. O'Malley not only discusses these in detail, but provides an Appendix for the levels of evidence for the CFF recommendations. Four principles are stressed: standard precautions, transmission-based precautions, hand hygiene, and care of respiratory equipment. It is essential for RTs caring for patients with CF to follow these infection-control recommendations. Cohorting patients infected with *Burkholderia cepacia* complex is an intervention that is successful at keeping the spread of this pathogen low. However, cohorting patients who are infected and/or colonized with other microbes is controversial. The main argument against cohorting is not being certain of a patient's present respiratory culture status at any given visit.

Inhaled antibiotics are commonly administered as part of the care of patients with CF. Aerosol antibiotics achieve high local concentrations in the airways and reduce systemic toxicity. They are used successfully for long-term suppressive treatment for established *Pseudomonas aeruginosa* infections. Aerosol antibiotics have also been tried for early eradication of *Pseudomonas aeruginosa* airway infection. As Geller indicates, the ideal treatment strategy is still being investigated. This is almost certainly an area that will change greatly in the years to come. Tobramycin solution for inhalation is currently the only approved inhaled antibiotic in the United States. Because the time burden for patients to receive inhaled tobramycin via jet nebulizer is substantial, efforts have focused on faster, more efficient delivery methods. In addition, novel formulations of aerosol antibiotics are being studied, including β -lactams, fluoroquinolones, and aminoglycosides. Phase 3 studies of aztreonam for inhalation have shown improved outcomes and a short delivery time. Liposome formulations are being studied as a way to penetrate mucoid biofilms and prolong the residence time of antibiotics in the lungs. Light, porous, dry-powder formulations are in clinical trials to reduce delivery time. Given the number of formulations and delivery systems currently under investigation, we will doubtless see the introduction of several of these in the near future, an eventuality that will surely impact care.