

# Editor's Commentary

In this issue, we are pleased to publish the papers from the 53<sup>rd</sup> RESPIRATORY CARE Journal Conference, "Aerosol Drug Delivery in Respiratory Care." We appreciate the efforts of the conference co-chairs Arzu Ari and Bruce Rubin. We also appreciate the contributions of the faculty, whose papers and contributions to the discussions have made this a successful conference.

The first paper, by Restrepo et al, addresses aerosolized antibiotics. Aerosol delivery ensures high concentrations of the medication in the lungs, with low levels of systemic absorption. Aerosolized antibiotics have been tested as treatment strategies for bacterial infections in subjects with cystic fibrosis (CF), non-CF bronchiectasis, and ventilator-associated pneumonia (VAP). The most successful application to date is treatment of infections in patients with CF. This review summarizes the available evidence supporting the use of aerosolized antibiotics.

Willson addresses the topic of aerosolized surfactants, anti-inflammatory agents, and analgesics. Aerosol delivery offers convenience, rapid onset of action, and avoidance of the needles and sterile technique necessary with intravenous drug administration. It may change the pharmacokinetics of many drugs, however, and an awareness of the caveats of aerosol drug delivery is mandatory to ensure safety and adequate drug delivery.

As reviewed by Hill et al, the inhaled route has a number of attractive features for treatment of pulmonary hypertension (PH). It might improve ventilation-perfusion matching, by dilating vessels supplying ventilated regions, and thus improve gas exchange. It may also achieve higher local drug concentrations at a lower overall dose, potentially reducing drug cost. Many inhaled agents for PH are prostacyclins used off-label as a continuously nebulized medication. Aerosolized iloprost and treprostilin are prostacyclins cleared by the FDA to treat pulmonary arterial hypertension (PAH). Inhaled nitric oxide (INO) is cleared for the treatment of PH of the newborn, but is used off-label to test acute vasoreactivity in PAH and to treat acute right heart failure in hospitalized patients.

Aerosol therapy now includes nucleic acids, peptides that target lung diseases, and peptides to treat diseases outside the lungs. The review by Laube focuses on these newer applications for aerosol therapy, providing the status of each and the challenges that remain to their successful development. Factors that affect the success of these agents include developing formulations that are safe to the lungs, improving delivery beyond the airway mucus barrier, developing efficient aerosol devices, developing devices that increase aerosol delivery to infants, optimizing the bioavailability of systemically delivered peptides, and developing peptide formulations for systemic delivery that do not cause changes in lung function.

There are a number of mucoactive medications that have been used in an attempt to reduce hypersecretion, make secretions easier to transport, or increase the efficiency of cough or mucociliary clearance. In his paper, Rubin reviews the pathophysiology of secretory hyperresponsiveness and mucus hypersecretion, and discusses aerosol medications that can be used to augment secretion clearance.

Berlinski describes the assessment of new technologies in aerosol medicine. Matching patient, drug, and device is a challenge. Patients and families need to participate in the selection of an appropriate device. Clinicians need comparative data to help them choose the right device. New devices and drugs can be compared to existing technology with in-vitro and in-vivo methods. Expensive device/drug manufacturers need to be able to justify coverage of new products by third party payers by showing a positive cost-benefit relationship. Post-market surveillance is necessary for old drugs with new devices or new drug/device to ensure patient safety.

Imaging techniques in aerosol medicine are described by Corcoran. Scintigraphy quantifies aerosol deposition and is performed using 2D planar, 3D positron emission tomography (PET), or single-photon emission computed tomography (SPECT) imaging techniques. SPECT and PET imaging provide better dose localization but quantification is more complex. Aerosols have been used to deliver radiopharmaceutical probes for measurements of ventilation, mucociliary and cough clearance, and liquid absorption in the airways. Clearance measurements have been used to assess therapeutic response in conditions like CF.

Ari reviews factors affecting aerosol drug delivery to mechanically ventilated adults and spontaneously breathing patients with artificial airways. Device selection, optimum technique with each device, and unmet medical needs in aerosol medicine and critical care are also discussed.

The purpose of the paper by Hess is to review the available evidence related to the use of inhaled aerosols with noninvasive ventilation (NIV) or high flow nasal cannula (HFNC). Available evidence supports the delivery of aerosols during NIV. Inhaled bronchodilator response might be improved with the use of NIV in acute asthma, but the evidence is not sufficiently mature to recommend this as standard therapy. Evidence does support that aerosols can be delivered without discontinuation of NIV in patients receiving this therapy. Regarding aerosol delivery during HFNC, clinical studies are needed and, based on the available in vitro evidence, it is not possible to recommend for or against aerosol delivery with HFNC.

The topic of device cleaning and infection control in aerosol therapy is reviewed by O'Malley. Aerosol delivery devices are semi-critical medical devices; infection prevention and control (IPC) guidelines recommend that they be cleaned, disinfected, rinsed with sterile water, and air-dried. Challenges lie in awareness of IPC guidelines and establishing a standard for the care of aerosol delivery devices among all stakeholders; manufacturers, government, vendors and users. Respiratory therapists (RTs) play a significant role in providing and teaching aerosol therapy to patients. All stakeholders need to work together to provide a standard of care for the safe use of aerosol delivery devices.

Ruppel reviews the use of aerosolized medications used in the pulmonary function laboratory. The two most common implementations are bronchodilators and bronchial challenge agents. Bronchodilator administration is not well standardized, largely because of the various methods of delivery. Metered dose inhalers used with spacer devices are the most common route for bronchodilator administration, but many laboratories use nebulizers. Protocols for administering bronchial challenge aerosols (methacholine, mannitol, hypertonic saline) are well defined but are susceptible to some of the same problems that limit comparison of bronchodilator techniques. Bronchochallenges with inhaled aerosols are influenced not only by the delivery device, but also by the patient's breathing pattern, particularly in protocols that include deep inspiratory efforts.

Patients who have not been trained or do not understand use of drug and device combinations often do not use an aerosol device correctly. Many patients have the competence to use the device correctly, and know why they should use the device correctly, but still contrive to use it in a suboptimal manner. Ensuring effective aerosol therapy also involves understanding why, when, and how to use their medication; patient competence to use the device; patient motivation to adhere to therapy; and not contriving to use the device in a way that prevents effective drug delivery. Ari suggests strategies to evaluate, monitor, and improve patient adherence.