2002). However, aerosolized pentamidine isethionate continues to be a popular agent for the prophylaxis of Pneumocystis carinii pneumonia. In the outpatient clinics of our pediatric hospital, it is not unusual for us to administer four or more pentamidine treatments on a given day. We have modified the Respirgard (Marquest Medical Products; Englewood, CO), the nebulizer system that was expressly specified by the US Food and Drug Administration for the delivery of pentamidine aerosol, by interfacing it to an airtight soft-cushion mask. This modification allows us not only to contain pentamidine aerosol within the confines of the mask, but also to trap any tuberculosis droplet nuclei that might be generated secondary to aerosol-triggered coughing. This is an important factor to consider when dealing with patients who are immunocompromised, and might unwittingly harbor active tuberculosis. So-called “pentamidine booths” have been created to cope with this hazard, but having a toddler sit in an airtight booth that isolates the child from his/her parents is not a practical alternative. In a sense, the airtight booth for the face.

When we tested the Respirgard circuit that had been modified in this manner, an unforeseen bonus was observed to emerge. Pentamidine deposition roughly doubled, owing to the fact that the mask apparently serves as a spacer or holding chamber. The Respirgard system, as supplied by the manufacturer, already incorporates a breathing circuit filter, the Marquest MQ-303. Admittedly, one’s ability to sequester particles, intended for the patient, within the circuit will be crucially linked to the competence of that filter. Unfortunately, one of our sharp-eyed RCPs noted that a faintly visible plume of pentamidine could be observed to traverse the MQ-303 filter during administration of that agent! For that reason, we require that our therapists mount an ultraefficient breathing circuit filter (Conserve 50; Fall Corporation; East Hills, NY) on the outlet of the MQ-303. Any reader who might be interested in learning the specifics of our methodology is invited to supply me with an e-mail address to which I will post an electronic file containing a thoroughly detailed slide show. This slide show, written as a portable document format (PDF) file, is readable using Adobe Acrobat Reader software (Adobe Systems Incorporated; San Jose, CA), which is itself downloadable, free of charge, from the Adobe Web site.

Clinicians have enough to think about as they pursue their day-to-day activities of administering care to patients. Worrying about potential exposure to aerosolized drugs, airborne pathogens, and/or endotoxins shouldn’t need to be added to our list of concerns. And, separate and distinct from that issue, drugs that are prescribed for patients should be taken by patients, and should not be shared by the practitioners who are obliged to be within arm’s length. I would respectfully suggest that this epitomizes the most literal and rigorous application of the “patient-centered care” ideal that constitutes the core of our clinical practice.

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Nasal Nitric Oxide

Clue to a Diagnosis of Ciliary Dyskinesia

Primary abnormalities of ciliary structure and function, termed primary ciliary dyskinesia (PCD), are often diagnosed late in adult and pediatric patients presenting with respiratory tract manifestations such as bronchiectasis, sinusitis, or with infertility. Accurate diagnosis requires the suspicion of clinicians, and referral to a specialist center with expertise in assessing ciliary ultrastructure by electron microscopy, and performing ciliary function studies. While no cure is available, once diagnosed, careful attention can be directed to minimizing
morbidity through measures such as bronchial clearance and prompt treatment of infection.\textsuperscript{1}

Nitric oxide (NO) was discovered in the late 1980s to be an essential biological mediator in diverse species and systems.\textsuperscript{2} This molecule is synthesized by a family of constitutive and inducible NO synthases. The nasal cavity and paranasal sinuses excrete concentrations of NO that can reach several parts per million, orders of magnitude higher than the lower airway.\textsuperscript{3} This exuberant synthesis of NO is sufficient for an important antibacterial and antiviral effect, perhaps ensuring sinus sterility in health. Of relevance here, NO also has been reported to modulate ciliary function. Inhalation via the nose, which conditions the inspirate with endogenous NO, has been reported to have discernible effects on ventilation-perfusion matching in the lung. This may represent an important physiologic mechanism controlling matching of ventilation to pulmonary blood flow, and supports parental advice to “breathe through your nose”! The measurement of nasal NO is described in an American Thoracic Society statement on exhaled and nasal NO measurement from 1999.\textsuperscript{4}

In this issue of \textit{CHEST} (see page 1054), Corbella et al measured nasal and exhaled NO in children with PCD proven by ciliary ultrastructure on electron microscopy and compared these to children with other lung conditions and healthy control subjects. Mean values for nasal NO in PCD were 13.7 parts per billion (ppb) [95% confidence limit, 6.8 to 27.8], compared to 132.7 ppb (95% confidence limit, 76.5 to 230.2) in non-PCD respiratory patients and 223.7 ppb (95% confidence limit, 175.5 to 285.2) for control subjects. Others have also reported similar findings as discussed by the authors. There are few tests that show such a profound contrast between health and disease. Exhaled NO did not differentiate between the three groups, although the numbers were smaller. A nasal NO < 105 ppb had a sensitivity of 94% and a specificity of 89% for proven PCD. A low nasal NO has also been reported in cystic fibrosis, non-PCD bronchiectasis, sinusitis, and panbronchiolitis, so a firm diagnosis requires examination of ciliary ultrastructure.

Aside from a marker of PCD, NO production may be involved in ciliary motility. Thus, the administration of NO donors\textsuperscript{5} and the precursor of NO, the amino acid L-arginine, have been reported to increase ciliary beat frequency, while inhibitors of NO synthase reduce ciliary beat frequency.\textsuperscript{6} Both inducible and constitutive NO synthase isoforms may be expressed in ciliated nasal epithelial cells.\textsuperscript{6} The low nasal NO could also be linked to a susceptibility to upper airway infection.

So where do we go from here? Nasal NO should be available in specialist centers, and should be measured with simple and foolproof standardized techniques.\textsuperscript{4,7} Larger studies should examine the utility for the diagnosis of PCD in patients with sinusitis and bronchiectasis by publishing ranges in health and disease. Careful controlled studies should examine whether therapeutic intervention to increase the levels of upper airway NO modulate ciliary function and if this improves clinical outcomes. Companies should endeavor to provide simple and cost-effective instruments to measure nasal NO and obtain regulatory medical device clearance with reimbursement codes. Awareness of PCD is being increased through the PCD Foundation (http://www.pcdfoundation.org). Registries of PCD patients will allow clinical trials to be performed and therapeutic agents to be validated for this rare but important set of conditions. Pharmaceutical companies may become interested if nasal NO augmentation, not only helps patients with PCD but also those with other abnormalities of ciliary function whether primary or secondary.

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