Fig. 2. Two high-efficiency particulate air (HEPA) filters are placed in sequence in the expiratory limb. The proximal filter with the highest exposure to ribavirin is discarded after 1 h of ribavirin therapy for each dose. The new HEPA filter is placed distal to the existing filter such that the filter that was previously in the distal position moves into the proximal position.

istered, the circuit was disconnected up to 3 times: once to remove the proximal HEPA filter and insert a new distal one, once to remove the vibrating mesh micropump for cleaning, and last to replace the vibrating mesh micropump after cleaning. This patient was able to tolerate the interruption in ventilator support without desaturation. He successfully extubated after 6 days and shortly thereafter discharged from the ICU.

Ribavirin delivery has some well recognized complications when administered during mechanical ventilation. These include occlusion of the ventilator circuit with crystalline deposits and the use of additional inspiratory flow to achieve delivery that impedes patients' ability to trigger the ventilator and often requires increased sedation and sometimes neuromuscular blockade for tolerance. The vibrating mesh micropump does not require the addition of inspiratory flow to deliver ribavirin, unlike the small-particle aerosol generator-2 (SPAG-2).[2] This allowed our patient to continue a spontaneous mode of ventilation with appropriate triggering and accurate tidal volume measurement. Use of the vibrating mesh micropump did not prevent circuit occlusion with crystallized ribavirin, but this issue was easily solved with additional sterile water flushes, as described above. Based on the findings of Walsh et al,[1] 0.9% NaCl could also have been used to minimize the risk of pulmonary irritation. We hypothesize that the use of a syringe to deliver ribavirin through the vibrating mesh micropump should reduce the exposure of health-care providers to ribavirin compared with the SPAG-2, where the medication needed to be poured into the reservoir before delivery, but this has not yet been studied.

Conclusions from Walsh et al[1] suggest that utilization of a vibrating mesh micropump within the ventilator circuit can deliver similar amounts of ribavirin as the SPAG-2 delivery system but without the addition of a significant amount of additional inspiratory flow that can complicate ventilator management. We confirm this observation in a pediatric patient and add pragmatic information about one method of delivering inhaled ribavirin using a vibrating mesh micropump using additional expiratory filters during mechanical ventilation.

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REFERENCES

1. Walsh BK, Betit P, Fink JB, Pereira LM, Arnold J. Characterization of ribavirin aerosol with small particle aerosol generator and vibrating mesh micropump aerosol technologies. Respir Care 2016;61(5):577-585.
2. Guerguerian AM, Gauthier M, Lebel MH, Farrell CA, Lacroix J. Ribavirin in ventilated respiratory syncytial virus bronchiolitis. Am J Respir Crit Care Med 1999;160(3):829-834.
3. Chu HY, Renaud C, Ficken E, Thomson B, Kuypers J, Englund JA. Respiratory tract infections due to human metapneumovirus in immunocompromised children. J Pediatric Infect Dis Soc 2014;3(4):286-293.
4. Egli A, Bucher C, Dumoulin A, Stern M, Buser A, Bubendorf L, et al. Human metapneumovirus infection after allogeneic hematopoietic stem cell transplantation. Infection 2012;40(6):677-684.
5. Dokos C, Masjosthusmann K, Rellensmann G, Werner C, Schuler-Lüttmann S, Müller KM, et al. Fatal human metapneumovirus infection following allogeneic hematopoietic stem cell transplantation. Transpl Infect Dis 2013;15(3):E97-E101.
6. Shah DP, Ghantoji SS, Mulanovich VE, Ariza-Heredia EJ, Chemaly RF. Management of respiratory viral infections in hematopoietic cell transplant recipients. Am J Blood Res 2012;2(4):203-218.
7. Molinos-Quintana A, Pérez-de Soto C, Gómez-Rosa M, Pérez-Simón JA, Pérez-Hurtado JM. Intravenous ribavirin for respiratory syncytial viral infections in pediatric hematopoietic SCT recipients. Bone Marrow Transplant 2013;48(2):265-268.
8. Kitanovski L, Kopriva S, Pokorn M, Dolničar MB, Rajić V, Stefanović M, Jazbec J. Treatment of severe human metapneumovirus (hMPV) pneumonia in an immunocompromised child with oral ribavirin and IVIG. J Pediatr Hematol Oncol 2013;35(7):e311-e313.
9. Shahda S, Carlos WG, Kiel PJ, Khan BA, Hage CA. The human metapneumovirus: a case series and review of the literature. Transpl Infect Dis 2011;13(3):324-328.

Next Logical Step

I appreciate Hartmann and colleagues' letter outlining the next logical step of our

bench study,[1] a clinical trial of the use of the vibrating mesh micropump technology for ribavirin delivery. Although the use of aerosolized ribavirin remains controversial, the patient selection by Hartmann et al appears to be on target with the latest supporting evidence of potential benefit. Therapies offered within respiratory care are without conclusive evidence. In these cases, it is a balance of risk versus benefit. For the most part, many of the therapies we provide are low risk, and therefore the smallest of beneficial therapies are studied in clinical trials.

Continuous aerosol delivery in the mechanically ventilated patient with traditional jet nebulizers or in the case of ribavirin delivery via the small-particle aerosol generator (SPAG) can place the patient at additional risk of complications for a host of reasons surrounding the addition of flow within the ventilator circuit. Respiratory therapists for years have compensated for this known complication by being physically present during intermittent aerosol drug delivery to provide a near continuous clinical assessment and if necessary intervention. This continuous assessment is not possible when these treatments are prolonged past the traditional 10–15 min timeframe.

Since the introduction of the vibrating mesh micropump technology, the capability to monitor pulmonary mechanics and ventilator operation during aerosol delivery is possible, because the vibrating mesh micropump does not add additional flow to the circuit. This improves the safety profile of this delivery method. The vibrating mesh micropump may provide a safer delivery with similar results to that of SPAG, but we cannot ignore the many unknowns of this drug therapy, nor should we let the use of this proposed delivery method blindly open the door for widespread application without further study. Let's review a couple of unknowns mentioned in the letter. First, the team switched ventilators according to a manufacturer recommendation. This introduces a variation in practice, circuit change, and exposes the patient with ARDS to a disconnect from the ventilator circuit. Was this really necessary, because the team was properly filtering the expiratory gases? Second, the team quickly identified crystallization after the 22 mL (2-h drug delivery), which lead them to change their practice and rinse after each therapy session. This again led to a disconnection in an immunocompromised patient with severe lung disease. Disconnects in mechanically ventilated patients have been associated with a hypoxia related to a decrease in functional residual capacity, and they potentially increase the chances of ventilator-associated pneumonia. The crystallization found also raises the question of loss of drug delivery and where else it may have been building up that was not seen. Could it be in the endotracheal tube? Not turning the humidifier off likely reduced the crystallization after humidifier use to that seen before humidifier use. Third, the team felt the need to double filter the expiratory limb with good intentions of protecting the integrity of the expiratory valve, transducers, and clinicians. However, the rationale of using 2 identical high-efficiency particulate air (HEPA) filters designed to filter to the same micron particle level does not appear to be logical. This likely only adds resistance to expiratory flow and potentially exposes the patient to an additional risk. Changing a single HEPA filter following the 2-h aerosol delivery would have alleviated concerns of an incompetent filter. Last, although this case had an outcome we all would hope for, it is not clear whether this was the result of the aerosolized ribavirin therapy or a combination of efforts.

We are a profession known to deliver low-volume, high-risk therapies well. Yet, we must consider the risk of every intervention and look beyond our 4 walls to determine whether there is a better method on the horizon. I applaud the Hartmann group's use of the Journal and for assessing the risk and benefits in this extreme situation. They appropriately interpreted our study and logically chose the more frequently used and perceived safer vibrating mesh micropump over the less frequently utilized and potentially higher risk SPAG device. Their critical analysis of the literature allowed them to choose the appropriate patient, drug, and device, leading to a safe delivery of the potentially beneficial aerosolized ribavirin and overall wonderful care.

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REFERENCE

1. Walsh BK, Betit P, Fink JB, Pereira LM, Arnold J. Characterization of ribavirin aerosol with small particle aerosol generator and vibrating mesh micropump aerosol technologies. Respir Care 2016;61(5):577-585.

Airway Pressure Release Ventilation May Result in Occult Atelectrauma in Severe ARDS

To the Editor:

In a recent issue of RESPIRATORY CARE, Mireles-Cabodevila and Kacmarek[1] did an excellent job reviewing the pros and cons of airway pressure release ventilation (APRV). The paper and the discussion session raised serious concerns about ARPV, particularly regarding imposed work of breathing and excessive tidal volumes due to high peak transpulmonary pressures. However, neither in the paper (except for a brief reference by Dr Mireles-Cabodevila) nor in the discussion was there an emphasis on what we believe is the most dangerous risk of using APRV as a rescue treatment for severe ARDS: occult atelectrauma.

Although the use of APRV has almost disappeared at our institution (Cleveland Clinic), a few years ago there was a lot of interest in the mode. As a result, we got involved in some research on the topic, producing a few papers and abstracts. What always intrigued us was the frequent justification by supporters for using APRV that "it works," meaning that oxygenation improved in patients with severe ARDS, yet patients with severe ARDS rarely die of hypoxemia (~10%); they die of multi-organ failure. Organ failure is linked to the release of inflammatory mediators from the lung in response to mechanical trauma. Hence, focusing on oxygenation as the main goal of APRV at the expense of lung-protective ventilation does not seem like the most rational approach.

Oxygenation problems are usually managed with PEEP. Patients with severe ARDS should have end-expiratory lung volume manipulated by some form of optimal PEEP heuristic. However, the most vehement supporters for APRV recommend setting zero PEEP (ie, P_{low} = 0 cm H_2O but setting T_{low} short enough to maintain adequate end-expiratory lung volume by means of auto-PEEP).[2] However, reliance on auto-PEEP instead of set PEEP may result in unknown and unstable lung volumes and hence unstable mechanical support of gas exchange (not to mention the uneven distribution of auto-PEEP in the lungs according to the dis-