Lung edema clearance: 20 years of progress

This year marks the 20th anniversary of the publication of a landmark paper by Dr. Michael Matthay and colleagues in the Journal of Applied Physiology that proved to be pivotal in the study of lung edema clearance. To honor this achievement, I am pleased to introduce the newest Highlighted Topics series entitled, “Lung Edema Clearance: 20 Years of Progress.” In addition to featuring original research articles in this important area of investigation, we have invited several related review articles. The paper by Matthay and colleagues is an example of the high-quality research that is published in the Journal of Applied Physiology having substantial enduring impact. For example, there have been ~20 citations to this article in the past 2 years alone.

The 1982 Matthay et al. article (1) provided the first in vivo evidence that active transport mechanisms were likely to be responsible for removal of edema fluid from the distal air spaces of the lung across the tight alveolar epithelium. Dr. Matthay studied anesthetized, ventilated sheep that were surgically prepared to measure pulmonary and systemic hemodynamics, as well as lung lymph flow. To simulate the clinical problem of alveolar edema, an isosmolar solution of autologous serum was instilled with a fiberoptic bronchoscope into the distal air spaces of one lung. At the end of 4 h, the water volume of the instilled fluid was reduced by approximately 25–30%, as measured by standard gravimetric methods. Most importantly, the protein concentration of the serum instilled into the distal air spaces of the lung increased by approximately 30% above the concentration of the instilled serum (from 6.2 g/100 ml to 8.4 g/100 ml). The protein concentration in the distal air spaces of the lung was higher than the concentration of the instilled serum (from 6.2 g/100 ml to 8.4 g/100 ml). The protein concentration in the distal air spaces of one lung. At the end of 4 h, the water volume of the instilled fluid was reduced by approximately 25–30%, as measured by standard gravimetric methods. Most importantly, the protein concentration of the serum instilled into the distal air spaces of the lung increased by approximately 30% above the concentration of the instilled serum (from 6.2 g/100 ml to 8.4 g/100 ml). The protein concentration in the distal air spaces of the lung was higher than the concentration of the instilled serum (from 6.2 g/100 ml to 8.4 g/100 ml). The protein concentration

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also discuss the major changes in lung function that occur at birth.

In November, a mini-review entitled “Biophysical properties of Na\(^+\) channels in lung alveolar epithelial cells” by Drs. Matalon, Lazrak, Jain, and Eaton examines a variety of amiloride-sensitive, sodium-permeable channels in alveolar type II cells. The diversity of these channels may play a significant role in both normal lung physiology and pathophysiological states. Also in November, a mini-review entitled “Lung edema clearance: role of Na-K-ATPase” by Drs. Sznajder, Factor, and Ingbar explores the mechanisms of Na-K-ATPase regulation in the alveolar epithelium during lung injury. Alveolar epithelial Na-K-ATPase impacts the ability of the lung to clear edema, when Na-K-ATPase is inhibited or increased. These authors also raise many related questions about the ability of the lung to clear edema by modulating Na-K-ATPase activity.

In December, a mini-review entitled “Role of aquaporin water channels in fluid transport in lung and airways” by Drs. Borok and Verkman explores aquaporin water channels that are expressed in the airway and lung, where they facilitate osmotically driven water movement between the air space and capillaries. These authors also raise many related questions about the role of aquaporins that beg future study. Also in December, a mini-review entitled “Alveolar edema fluid clearance in the injured lung” by Drs. Berthiaume, Folkesson, and Matthay summarizes how alveolar edema fluid clearance occurs in the injured lung. This mini-review provides a concise perspective of experimental and clinical studies, which demonstrate the importance of active ion transport mechanisms in the removal of edema fluid after clinically relevant acute lung injury.

Until Dr. Matthay’s landmark article (1), the idea that salt and water flux from alveoli could be regulated by active transport was hardly considered. Indeed, investigators ignored evidence that should have raised this possibility. At the time, it was appreciated that “passive” Starling forces played an important role in fluid filtration. Therefore, it only seemed logical to conclude that fluid clearance also occurred by the same mechanism but in the reverse order. For this reason, it was troubling to learn that the alveolus seemed to be rather impermeant to the movement of water and solute. Restoration of “normal” Starling forces did not drive fluid back into the interstitium at a rate that would have been predicted based on fluid filtration coefficients. Dr Matthay’s seminal observation that the lung “concentrates” protein labels in alveolar fluid clearly pointed out the reason for this phenomenon. Two decades later, we have learned quite a lot about alveolar edema clearance. We now know that alveolar water and salt transport is regulated by ion channels and pumps. Expression and activity of these membrane proteins are altered in disease and can be experimentally manipulated. Needless to say, compounds with actions on channel and pump proteins are attractive candidates for treating patients with pulmonary edema. Although the efficacy of clearance targeted interventions has yet to be established in clinical trials, several such trials are underway and will add a chapter to the bench to bedside story that was begun by Dr. Matthay some 20 years ago. This study epitomizes the translational physiology that has been the long-standing tradition of research published in the Journal of Applied Physiology. A major purpose of this and any Highlighted Topics series is to draw attention to the importance of such research and to encourage future submissions in translational physiology.

REFERENCES


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