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Study provides new insights into deadly acute respiratory distress syndrome

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This Image shows the lung surfactant, a complex composed of fats and proteins generated in the lungs, after being exposed to the lysolipid in water where the bright red spots indicate the lysolipid replacing the lung surfactant in a layer of cells. Credit: Zasadzinski Research Group, University of Minnesota Twin Cities

Researchers at the University of Minnesota Twin Cities may have discovered a mechanical explanation for instability observed in the lungs in cases of acute respiratory distress syndrome (ARDS), particularly in the aftermath of respiratory illnesses such as COVID-19 or pneumonia.

The research, "Evolution of interfacial mechanics of lung surfactant mimics progression of acute respiratory distress syndrome," was published in the Proceedings of the National Academy of Sciences (*PNAS*).

Currently, there is no known cure for ARDS, a life-threatening lung injury that allows fluid to leak into the lungs. The researchers in this study say that as many as two-thirds of all patients that passed away from COVID-19 had ARDS. There is not a clear reason why specific people with a severe respiratory illness may develop ARDS, while others may not, but researchers in this study were looking to find that answer.

They identified the concentration of a lysolipid—a byproduct of the immune response to viruses and bacteria—that can have a major impact in adults suffering from ARDS. Increased concentration of this chemical eliminates the surfactant, a complex composed of fats and proteins generated in the lungs. The result is uneven lung inflation and, ultimately, respiratory distress in adults.

"This study looked into the correlation of the concentration of the lysolipid in the lungs. Once that fluid reached a certain level, it started to cause severe impacts," said University of Minnesota Department of Chemical Engineering and Materials Science Professor Joseph Zasadzinski and lead professor on the research.

"Your average everyday person usually won't need to think about this, but if a virus or infection is bothering your lung surfactant system and you end up in the hospital, then it could become top of mind very quickly," Zasadzinski added

There are a natural amount of these lysolipids that exist in the human body, and as long as those stay below a specific concentration, the average person can breathe normally. When someone has a bad infection, those lysolipids increase, which can lead to respiratory distress. Once a patient is headed in that direction, there are not many ways of reversing those symptoms.

"This research shows frequency dependence, or how quickly you open and close the lungs. This could help doctors try to tailor the treatment process for each specific patient," said Clara Ciutara, a 2023 Ph.D. chemical engineering and materials science graduate and first author of the study.

Previous research on neonatal respiratory distress syndrome (NRDS) in premature infants found that it could be treated by introducing replacement lung surfactant, but that was not the case in adults. It is the amount of lysolipid that determines the outcome of the surfactant in the lungs, not the breakdown of the existing lung surfactant.

The next step in the research will be to translate these ideas into a clinical environment and test to see if they can manipulate specific molecules to make them less active or stick to a specific place. This could help drop the concentration of the lysolipids to a threshold that may be able to reverse symptoms of ARDS and put people on the road to recovery.

In addition to Zasadzinski and Ciutara, the research team included University of Minnesota Department of Chemical Engineering and Materials Science NIH postdoctoral fellow Steven V. Iasella, undergraduate student Boxun Huang, and former postdoctoral associate Sourav Barman.

A commentary piece on the research can also be found on the *PNAS* website.

More information: Clara O. Ciutara et al, Evolution of interfacial mechanics of lung surfactant mimics progression of acute respiratory distress syndrome, *Proceedings of the National Academy of Sciences* (2023). DOI: 10.1073/pnas.2309900120

Charles Maldarelli, Respiratory distress when a lung surfactant loses one of its two hydrophobic tails, *Proceedings of the National Academy of Sciences* (2024). DOI: 10.1073/pnas.2320426121

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