Acute respiratory distress syndrome

Acute respiratory distress syndrome (ARDS) is a medical condition occurring in critically ill or critically wounded patients characterized by widespread inflammation in the lungs. ARDS is not a particular disease; rather, it is a clinical condition triggered by various pathologies such as trauma, pneumonia, and sepsis.

The hallmark of ARDS is diffuse injury to cells which form the barrier of the microscopic air sacs of the lungs, surfactant dysfunction, activation of the innate immune system response, and dysfunction of the body's regulation of clotting and bleeding. In effect, ARDS impairs the lungs' ability to exchange oxygen and carbon dioxide with the blood across a thin layer of the lungs' microscopic air sacs known as alveoli.

The syndrome is associated with a death rate between 20 and 50%.

The risk of death varies based on severity, the person's age, and the presence of other underlying medical conditions.

Although the terminology of “adult respiratory distress syndrome” has at times been used to differentiate ARDS from “infant respiratory distress syndrome” in newborns, the international consensus is that “acute respiratory distress syndrome” is the best term because ARDS can affect people of all ages.

Neutrophil influx is a hallmark of ARDS and is associated with the release of tissue-destructive immune effectors, such as matrix metalloproteinases (MMPs) and membrane-anchored metalloproteinase disintegrins (ADAMs). Here, we observed using intravital microscopy that Adam8-/- mice had impaired neutrophil transmigration. In mouse pneumonia models, both genetic deletion and pharmacologic inhibition of ADAM8 attenuated neutrophil infiltration and lung injury while improving bacterial containment. Unexpectedly, the alterations of neutrophil function were not attributable to impaired proteolysis but resulted from reduced intracellular interactions of ADAM8 with the actin-based motor molecule Myosin1f that suppressed neutrophil motility. In 2 ARDS cohorts, we analyzed lung fluid proteolytic signatures and identified that ADAM8 activity was positively correlated with disease severity. We propose that in acute inflammatory lung diseases such as pneumonia and ARDS, ADAM8 inhibition might allow fine-tuning of neutrophil responses for therapeutic gain [1)]

[1)]
Conrad C, Yildiz D, Cleary SJ, Margraf A, Cook L, Schlomann U, Panaretou B, Bowser JL, Karmouty-Quintana H, Li J, Berg NK, Martin SC, Aljohmani A, Moussavi-Harami SF, Wang KM, Tian JJ, Magnen M, Valet C, Qiu L, Singer JP, Eltzschig HK; CAPSys Study Group, Bertrams W, Herold S, Suttorp N, Schmeck B, Ball ZT, Zarbock A, Looney MR, Bartsch JW. ADAM8 signaling drives neutrophil migration and ARDS severity. JCI Insight. 2022 Feb 8;7(3):e149870. doi: 10.1172/jci.insight.149870. PMID: 35132956.