Inflammatory pathways and microvascular responses in the lung

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Abstract:
Neutrophil granulocytes constitute an important host defense mechanism, but may at the same time damage functional tissue and propagate acute organ failure. This balance is particularly vulnerable in the lung which provides a large surface area for invading pathogens and microorganisms, and simultaneously harbors a large pool of physiologically marginated neutrophils within its microvascular bed. Pathophysiological stimuli further amplify this accumulation of blood cells and promote the emigration of neutrophils into the pulmonary interstitium and the airspaces by different mechanisms depending on the pathophysiological stimulus, its route of entry into or site of production in the lung, and the time course of its action. Importantly, the pulmonary microvascular endothelium plays a key role in regulating not only sequestration and emigration of neutrophils, but by initiating the inflammatory response to a variety of diverse stimuli many of which do not directly target the circulating neutrophil, but elicit microvascular reactions by primarily acting on the endothelium. This review highlights the inflammatory process in the pulmonary microvasculature with special emphasis on the role of the pulmonary endothelium.

Key words:
lung, inflammation, endothelium, neutrophil, margination, emigration

Introduction

The large alveolar surface area of approximately 80–140 m² [96] is in constant exchange with the ambient environment and thus, provides an ideal entry portal for the invasion of foreign material or biological pathogens including bacteria, toxic gases, and ultrafine or microparticles. The upper airways have developed a large set of defense mechanisms in order to minimize pathogen entry into the alveolar space including mechanisms of mechanical sequestration in the nasopharynx, the mucociliary escalator [94], the production of a bactericidal mucus containing lactoferrin, lysozyme, rhodanide ions, and immunoglobulins [44], and the secretion of salt-sensitive defensins into the airway lumen where they become activated by low-salt liquid on airway surfaces [30]. Pathogen invasion into the lower airspaces results in a pro-inflammatory activation of macrophages, epithelial and endothelial cells constituting the alveolo-capillary unit, and the recruitment of leukocytes – predominantly neutrophil granulocytes – from the blood into the airspace.

Neutrophil granulocytes, however, also bear the potential to damage normal host lung tissue under a variety of pulmonary or systemic pro-inflammatory conditions [36, 60]. This pathological situation com-