Commentary

Another piece in the puzzle

Thomas S Maxey[1] and William B Keeling[2]

[1]Chief Resident, General Surgery, Department of Surgery, University of South Florida College of Medicine, Tampa, Florida, USA
[2]Senior Resident, General Surgery, Department of Surgery, University of South Florida College of Medicine, Tampa, Florida, USA

Corresponding author: Thomas S Maxey, tjmaxey@yahoo.com

Published online: 9 December 2004
This article is online at http://ccforum.com/content/9/1/27

Critical Care 2005, **9**:27-28 (DOI 10.1186/cc3019)

See *Research* by Van Putte *et al*., page 119

Abstract

Pulmonary ischemia–reperfusion injury is complex and involves many cell types and mechanisms of action. Van Putte and coworkers have attempted to provide insight into and describe some of the complex components of this process. Their study describes two new components of the multifaceted process of reperfusion injury. The time-dependent course of neutrophil activation and the discovery of programmed cell death in reperfused lung tissue are two new pieces of a complex puzzle.

Keywords ischemia–reperfusion injury, lung injury, pulmonary

The multifaceted phenomenon of pulmonary ischemia–reperfusion (IR) involves alveolar macrophages, vascular endothelial cells, circulating neutrophils, adhesion factors, free radicals, and a wealth of cytokines. There is a large body of literature describing techniques to attenuate lung IR injury. To date, however, little attention has been focused on the specific mechanisms of lung IR injury itself. The complexity and amplification of the cascades involved in this phenomenon have made investigation of individual components of reperfusion injury difficult to assess.

Characterization of the injury pattern during the early phase of reperfusion is limited. Van Putte and colleagues [1] have attempted to provide insight into and describe some of the key components of this process using a warm blood perfused model. Fiser and coworkers [2] recently described the biphasic nature of reperfusion injury after lung transplantation, beginning with a resident (donor) macrophage response followed by a more intense response of circulating (recipient) neutrophils. Evidence that neutrophils play an important role in lung reperfusion injury has been reported by investigators using leukocyte depletion techniques as well as antibodies directed at adhesion molecules [3,4]. In contrast, some investigators have demonstrated that significant IR injury can occur without neutrophil participation, and in fact neutrophils may have no effect at all in some models of lung injury [5]. Our group [6] recently utilized a model that eliminates the role of circulating neutrophils altogether and allowed us to focus strictly on resident macrophages in the lung.

Despite the controversy surrounding the exact role played by circulating neutrophils, they are a critical component of the inflammatory cascade. The study by Van Putte and colleagues [1] clearly demonstrates a specific bimodal, time-dependent course for neutrophil infiltration (30 mins and 3 hours) after reperfusion. This new finding suggests that there is not only a recruitment phase of neutrophils but also a time-dependent activation phase.

The identification of apoptosis within pulmonary IR injury is perhaps one of the more significant findings in the experiment [1]. Although this particular study did not investigate the cell signaling mechanisms that are involved in programmed cell death, future studies will certainly better define this mechanism.

Van Putte and coworkers [1] successfully utilized a warm pulmonary IR model to investigate very specific components of a complex physiologic process. Their study verifies some

IR = ischemia–reperfusion.

previously described mechanisms of pulmonary IR injury and sheds new light on other mechanisms. Although these findings may not have immediate clinical implications, they certainly add another piece to a complex puzzle.

Competing interests

The author(s) declare that they have no competing interests.

References

1. Van Putte, Kesecioglu J, Hendricks JMH, Persy VP, Van Marck E, Van Schil PEY, Debroe ME: **Cellular infiltrates and injury evaluation in a rat model of warm pulmonary ischemia-reperfusion.** *Crit Care* 2005, **9:**R1-R8.
2. Fiser SM, Tribble CG, Long SM, Kaza AK, Cope JT, Laubach VE, Kern JA, Kron IL: **Lung transplant reperfusion injury involves pulmonary macrophages and circulating leukocytes in a biphasic response.** *J Thorac Cardiovasc Surg* 2001, **121:**1069-1075.
3. Breda MA, Hall TS, Stuart RS, Baumgartner WA, Borkon AM, Brawn JD, Hutchins GM, Reitz BA: **Twenty-four hour lung preservation by hypothermia and leukocyte depletion.** *J Heart Transplant* 1985, **4:**325-329.
4. Ferro TJ, Gertzberg N, Selden L, Neumann P, Johnson A: **Endothelial barrier dysfunction and p42 oxidation induced by TNF-α are mediated by nitric oxide.** *Am J Physiol* 1997, **272:** L979-L988.
5. Steimle CN, Guynn TP, Morganroth ML, Bolling SF, Carr K, Deeb GM: **Neutrophils are not necessary for ischemia reperfusion injury of the lung.** *Ann Thorac Surg* 1992, **53:**64-73.
6. Maxey TS, Enlow RI, Gaston B, Kron IL, Laubach VE, Doctor A: **Tumor necrosis factor-alpha from resident lung cells is a key initiating factor in pulmonary ischemia-reperfusion injury.** *J Thorac Cardiovasc Surg* 2004, **127:**541-547.