European Respiratory Society
Annual Congress 2013

Abstract Number: 1358

Publication Number: P653

Abstract Group: 3.3. Mechanisms of Lung Injury and Repair

Keyword 1: ALI (Acute Lung Injury) **Keyword 2:** Mechanical ventilation **Keyword 3:** Inflammation

Title: High-stretch, but not atelectasis, causes systemic cytokine release by lung-marginated monocytes

Dr. Kenji 9741 Wakabayashi k.wakabayashi@imperial.ac.uk MD [1], Dr. Michael 9742 Wilson michael.wilson@imperial.ac.uk [1], Dr. Kate 9743 Tatham k.tatham@imperial.ac.uk MD [1], Dr. Kieran 9744 O'Dea k.odea@imperial.ac.uk [1] and Prof. Masao 9745 Takata m.takata@imperial.ac.uk MD [1]. [1] Section of Anaesthetics, Pain Medicine & Intensive Care, Imperial College London, London, United Kingdom, SW10 9NH .

Body: Introduction The proposed pathophysiology of ventilator-induced lung injury (VILI) includes overdistension (volutrauma) and repetitive collapse and reopening (atelectrauma) of lung units. Using an isolated perfused mouse lung, we investigated the physiological and inflammatory consequences of these two mechanisms of VILI. Methods Isolated buffer-perfused lungs were ventilated with one of three protocols for 3 hours (n=5 each): 'Control' (7ml/kg tidal volume (VT), PEEP (5cmH2O) and regular sustained inflation (SI)); 'Atelectasis' (7ml/kg VT, zero PEEP without SI; 'High-stretch' (30-32ml/kg VT, PEEP (3cmH2O) with SI). Results Both injurious ventilation protocols led to increased peak inspiratory pressure (PIP; $p<0.05$ vs. start) and lavage protein (Table). High-stretch, but not atelectasis, increased perfusate cytokines compared to control. These increases were attenuated by monocyte depletion (achieved by pretreating animals with clodronate-liposomes), particularly TNF which was virtually abolished (302±69 vs. 20±14pg/ml; $p<0.05$). Monocyte depletion also attenuated stretch-induced PIP increase ($p<0.05$) and tended to reduce lavage protein ($p=0.18$). Conclusion These results strongly suggest that volutrauma, but not atelectrauma, activates lung-marginated monocytes leading to systemic cytokine release, which is a critical factor for multiple organ failure in ventilated critically-ill patients. Our findings may provide a novel explanation why open lung strategy seemingly has limited mortality benefits.

	Control	High-stretch	Atelectasis
Lavage protein (mg/ml)	0.21±0.04	4.42±2.50*	4.92±1.47*
Perfusate KC (ng/ml)	1.26±0.74	7.65±1.81*	1.70±1.09
Perfusate TNF (pg/ml)	61±57	213±97*	51±61

*$p<0.05$ vs. Control