Reviewer's report

Title: High tidal volume mechanical ventilation-induced lung injury in rats is greater after acid instillation than after sepsis-induced acute lung injury, but does not increase systemic inflammation: an experimental study.

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Reviewer: Dan Benhamou

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MS: 4588853515578176

As Reviewer 1, I believe that the study is well performed and results interesting and that publication is worthwhile. However, as Reviewer 2, I am somewhat surprised by the absence of true controls, i.e. animals which would have received mechanical ventilation (high ad low Vt) and no lung injury.

I suggest that authors provide a better discussion on this point rather than asking them to add now two additional groups (or to reject the paper). Indeed, the discussion on this point is clearly insufficient. The authors state for example that it is well known that “HVt used in the present study (i.e. 15 ml/kg) does not injure normal lungs”. This is a surprising statement which, above all, is not referenced. In a paper published by the authors themselves, it was shown that in healthy rats, a Vt of 15 ml/kg was injurious to the lungs as determined by lung histology (Kuiper JW et al, Anesth Analg 2008). In rabbits, mechanical ventilation of normal lungs with Vt of 10 ml/kg is not injurious (Altemeier WA et al, Am J Physiol Lung Cell Mol Physiol 2004;287(3):L533-42) but in other studies in mice (Vanecker et al, Anesthesiology 2007 and 2008) 8 ml/kg caused an inflammatory reaction in healthy lungs. The reviewer finds unclear as why the authors state that 15 ml/kg (high Vt) is said to be non injurious.

Moreover, the level of Vt that is tolerable in animals with lung injury would lie somewhere between 6 ml/kg and 15 ml/kg. Bem et al have shown that in mice, Vt of 10 ml/kg enhances lung inflammation after pneumovirus infection (Am J Physiol Lung Cell Mol Physiol 2009;296(1):L46-56).

The Discussion section thus needs to be improved and to better present the previously published evidence that would support their choice of “high” and “low” Vt.

Additional minor comments and questions
• In general, use a single style (UK or US) along the whole paper as recommended.
• P6, L18: what is meant by “One animal was ventilated per experiment”?
• P8, Last paragraph and P9: Is the histology score validated? Has it been used in previous studies? If yes, provide references.
• P9, Results, 1st paragraph: The sentences describing the evolution and comparison of MAP are unclear. The reviewer dose not understand why it is stated that the sepsis group had a lower MAP that the HVt acid group at baseline: looking at Table 1 does not support this. Please comment.

• As well, MAP was lower at H4, MAP was lower in the HVt sepsis group than in others. However, if one looks at changes expressed in percent, this does not seem to be true anymore, as baseline values were different among groups.

• P12, 5 first lines: delete as these sentences have already been written in the previous paragraphs.

• What is decompartmentalization? Is this an accepted term?