we also investigated inflammatory local and systemic cytokine profiles and clinical resolution of infectious parameters. In fact, our results clearly show that neutrophil apoptosis is associated with lower proinflammatory cytokine levels and faster clinical stability. This is a finding that would probably not have been changed if we had obtained lung biopsies.

Another comment refers to transepithelial elimination of neutrophils during resolution of NCAP. The interesting proposed hypothesis of inflammatory resolution through egression of leukocytes is very attractive [3]. C.G.A. Persson and L. Uller argue that elimination of leukocytes from the airways with bronchial inflammation (transepithelial egression) is a mode of resolving inflammation. This challenging interpretation is nicely presented in human and animal models in asthma and chronic obstructive pulmonary disease. However in pneumonia, the acute inflammatory response of host against microorganisms is a completely different model of airway inflammation. In pneumonia, innate responses and alveolar macrophages orchestrate the inflammatory response in lung parenchyma, and neutrophils exit the pulmonary circulation at the capillary level, that is, mainly in alveolar air spaces. Obviously, our design was not directed to evaluate the neutrophil migration across the alveolar or epithelial lining, although this topic merits attention.

Referring to the comments that evidence of neutrophil apoptosis in inflammation resolution is not very strong, it is worth mentioning that our results and those from other researchers seem to indicate the contrary [4–6]. We have found a significant correlation between neutrophil apoptosis and pneumonia outcome. Our results agree with the comment made by MATUTE-BELLO and MARTIN [7], indicating that studies in humans suggest that neutrophil apoptosis is inhibited early in acute respiratory distress syndrome but returns to normal as inflammation resolves. These authors also indicate other steps that must be explored to understand all the process, but they were not the objective of our present work. DROEMANN *et al.* [8] have results in concordance with ours, and the differences in the rate of neutrophil apoptosis are probably due to the initial phase of pneumonia (24 h).

So, we consider that the study of cytokine patterns and neutrophil apoptosis in BAL fluid from NACP is currently an excellent available option to evaluate the ongoing inflammatory process *ex vivo*. With regard to the role of the transepithelial exit of leukocytes from the airway proposed by C.G.A. Persson and

L. Uller for asthma and chronic obstructive pulmonary disease, it should not be directly translated to pneumonia, an acute infection with a completely different *restitutio in integrum*. Finally, we totally agree that regarding the host response against microorganisms and resolution of inflammation, there are still many missing important pieces and new approaches are welcome.

I. Moret*, M.J. Lorenzo^{#,†,+}, B. Sarria* and R. Menendez^{#,†,+,§}

*Pharmacology Dept, School of Medicine, University of Valencia, [#]Pneumology Service, University and Polytechnic Hospital La Fe, [†]IIS La Fe-Fundacion Bancaya, [§]CIBER de Enfermedades Respiratorias (CIBERES), Valencia, and [†]Medicine-Doctoral Programme Dept, Barcelona Autonomous University, Barcelona, Spain.

Correspondence: R. Menendez, Pneumology Service, University and Polytechnic Hospital La Fe, Avda Bulevar sur s/n, 46026 Valencia, Spain. E-mail: rosmenend@gmail.com

Statement of Interest: None declared.

REFERENCES

- 1 Moret I, Lorenzo MJ, Sarria B, *et al.* Increased lung neutrophil apoptosis and inflammation resolution in nonresponding pneumonia. *Eur Respir J* 2011; 38: 1158–1164.
- 2 Menendez R, Torres A. Treatment failure in community-acquired pneumonia. *Chest* 2007; 132: 1348–1355.
- 3 Persson C, Uller L. Transepithelial exit of leucocytes: inflicting, reflecting or resolving airway inflammation. *Thorax* 2010; 65: 1111–1115.
- 4 DeLeo FR. Modulation of phagocyte apoptosis by bacterial pathogens. *Apoptosis* 2004; 9: 399–413.
- 5 Chopra M, Reuben JS, Sharma AC. Acute lung injury: apoptosis and signaling mechanisms. *Exp Biol Med* 2009; 234: 361–371.
- 6 Sookhai S, Wang JJ, McCourt M, *et al.* A novel therapeutic strategy for attenuating neutrophil-mediated lung injury *in vivo*. *Ann Surg* 2002; 235: 285–291.
- 7 Matute-Bello G, Martin TR. Science review: apoptosis in acute lung injury. *Crit Care* 2003; 7: 355–358.
- 8 Droemann D, Aries SP, Hansen F, *et al.* Decreased apoptosis and increased activation of alveolar neutrophils in bacterial pneumonia. *Chest* 2000; 117: 1679–1684.

DOI: 10.1183/09031936.00217511

Chest radiotherapy to achieve lung volume reduction

To the Editors:

We read with great interest the letter from O'MEARA *et al.* [1] regarding the mechanism of dyspnoea relief following radiation treatment in a patient with severe chronic obstructive pulmonary disease and presumed bronchogenic malignancy. Our group has long been interested in the potential for lung radiotherapy to noninvasively result in lung volume reduction, after we have observed dyspnoea relief in similar patients. The clinical and physiological benefit of lung volume reduction in select patients with obstructive lung disease has been demonstrated. The

benefits of lung volume reduction surgery, however, are offset by the surgical morbidity. Varied non-surgical and bronchoscopic procedures are under evaluation, including endobronchial valves, biological agents, thermal airway ablation and airway bypass. Unfortunately, the goal of collapsing overinflated emphysematous lung with non-surgical techniques has had mixed results to date [2–4].

We propose (again) that lung radiotherapy has similar potential physiological benefit in patients similar to those presented by O'MEARA *et al.* [1], and this is an area which is ripe for clinical

research. Since the work of AXFORD *et al.* [5], there has been very limited published work along this topic, despite the fact that the technical understanding of lung radiotherapy has advanced considerably. A model can be conceived in which dose and fractionation are designed to limit the syndrome of pneumonitis, and resulting in regional fibrotic shrinkage. We agree with the proposed mechanism of the authors, believe that this is an area which is ripe for clinical research and call for a broad discussion on this topic.

J.A. Murray and J. Lyons

Unity Health System, Rochester, NY, USA.

Correspondence: J.A. Murray, Unity Health System, 1561 Long Pond Road, Suite 408, Rochester, NY, 14626, USA. E-mail: jmurray01@unityhealth.org

Statement of Interest: None declared.

REFERENCES

- 1 O'Meara P, Guenette JA, Raghavan N, *et al.* Mechanisms of dyspnoea relief following radiation treatment in a patient with severe COPD. *Eur Respir J* 2011; 38: 728–730.
- 2 Sciruba FC, Ernst A, Herth FJ, *et al.* A randomized study of endobronchial valves for advanced emphysema. *N Engl J Med* 2010; 363: 1233–1244.
- 3 Berger RL, Decamp MM, Criner CJ, *et al.* Lung volume reduction therapies for advanced emphysema: an update. *Chest* 2010; 138: 407–417.
- 4 Snell GI, Hopkins P, Westall G, *et al.* A feasibility and safety study of bronchoscopic thermal vapor ablation: a novel emphysema therapy. *Ann Thorac Surg* 2009; 88: 1993–1998.
- 5 Axford AT, Cotes JE, Deeley TJ, *et al.* Clinical improvement of patients with emphysema after radiotherapy. *Thorax* 1977; 32: 35–39.

DOI: 10.1183/09031936.00192511

From the authors:

We thank J.A. Murray and J. Lyons for their insightful comments on our recent case report dealing with dyspnoea relief in a patient with chronic obstructive pulmonary disease (COPD) and presumed lung cancer following radiation treatment [1]. Despite the impressive improvements in symptoms, exercise tolerance and pulmonary function in our patient, we cannot generalise our findings to the COPD population as a whole. Clinical experience has taught us that radiation-induced toxicity, when superimposed on the baseline respiratory impairment of COPD, may lead to further clinical deterioration in some patients. Thus, it is well established that radiation injury to the lungs initiates a cascade of events that create a self-sustaining cycle of chronic oxidative stress and inflammation [2]. Inflammation of the airways, pulmonary vasculature and lung parenchyma ultimately results in negative effects on pulmonary gas exchange (something we also observed in our patient). Nevertheless, some

patients may, paradoxically, derive symptomatic improvement due to radiation-induced lung deflation [1, 3], but this response is likely to be variable given the vast pathophysiological heterogeneity of COPD.

There is a paucity of data on the effects of modern radiotherapy techniques on detailed respiratory physiology, exercise performance and respiratory symptoms in patients with combined COPD and lung cancer. Before we can even consider radiotherapy as a noninvasive alternative to lung volume reduction surgery, we need to refine selection criteria to help predict who is most likely to derive sustained symptomatic benefit. In order to do this, we need to be able to adequately characterise COPD phenotypes by comprehensive clinical evaluation, which includes detailed radiological and physiological assessment. This should be followed by a careful evaluation of both the short- and long-term effects of radiotherapy on respiratory symptoms, perceived health status, lung structure and function. We are therefore in agreement with J.A. Murray and J. Lyons that further study is required to determine whether radiotherapy-induced lung volume reduction can be considered in the management of selected patients with COPD and lung hyperinflation who report incapacitating dyspnoea.

J.A. Guenette*, N. Raghavan*, P. O'Meara*, C.E. de Metz* and D.E. O'Donnell*

*Respiratory Investigation Unit, Dept of Medicine, Queen's University and Kingston General Hospital, and #Cancer Centre of South Eastern Ontario, Kingston General Hospital, Kingston, ON, Canada.

Correspondence: J.A. Guenette, Respiratory Investigation Unit, Queen's University and Kingston General Hospital, 76 Stuart Street, Kingston, ON, Canada, K7L-2V6. E-mail: guenette@queensu.ca

Statement of Interest: A statement of interest for D.E. O'Donnell can be found at www.erj.ersjournals.com/site/misc/statements.xhtml

REFERENCES

- 1 O'Meara P, Guenette JA, Raghavan N, *et al.* Mechanisms of dyspnoea relief following radiation treatment in a patient with severe COPD. *Eur Respir J* 2011; 38: 728–730.
- 2 Ghafoori P, Marks LB, Vujaskovic Z, *et al.* Radiation-induced lung injury. Assessment, management, and prevention. *Oncology (Williston Park)* 2008; 22: 37–47.
- 3 Axford AT, Cotes JE, Deeley TJ, *et al.* Clinical improvement of patients with emphysema after radiotherapy. *Thorax* 1977; 32: 35–39.

DOI: 10.1183/09031936.00205211