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# The lungs are not a lonely island — a current view on respiratory diseases

*Pneumonol. Alergol. Pol.* 2011; 79, 3: 165–166

Studies investigating the mechanisms responsible for the development and progression of respiratory diseases conducted in recent years but also the state-of-the-art and increasingly sophisticated technologies that successfully allow us to gain an insight into the structure of the lungs and the microcosm of cells and tissues have become a driving force for the key changes in contemporary opinions on the processes which eventually shape the clinical picture and complaints that prompt the patient to seek a pulmonologist consultation. Although the postgraduate education system does promote narrow medical specialisation restricted to specific organs and systems, the conclusions drawn from research studies as well as clinical analyses and observations made by individual medical practitioners increasingly point to the systemic nature of many pulmonary diseases previously perceived as pathologies more or less confined to the respiratory system only. The systemic nature is currently attributed to acute and chronic diseases of pulmonary origin. Chronic obstructive pulmonary disease (COPD) is currently regarded as a disorder of not only alveoli and bronchi. Chronic systemic inflammation, whose features are observed in most COPD patients, is known to result in changes in, for example, respiratory muscles (atrophy) and vascular endothelium, which in turn increases cardiovascular risk [1]. The systemic impact of acute inflammation, as in pneumonia, for example, seems obvious. Much less focus is, however, received by extrapulmonary effects of primary lung malignancies. Both issues have been

analysed, although from a different perspective, by authors of the original papers recently published in “*Pneumonologia i Alergologia Polska*”. Urbaniak et al. assessed selected parameters of inflammation, both local and systemic, in two groups: patients with community-acquired pneumonia and patients with pneumonia co-existing with lung cancer [2]. They compared the levels of free oxygen radicals ( $H_2O_2$ ), proinflammatory cytokines (tumour necrosis factor- $\alpha$  [TNF- $\alpha$ ]) and growth factors (vascular endothelial growth factor [VEGF]) in peripheral blood and in exhaled breath condensate and demonstrated significant differences between the study groups. While systemic levels of the cytokines (levels measured in peripheral blood) were significantly higher in patients with community-acquired pneumonia, the opposite was the case in the material obtained directly from the airways. The levels of the markers in exhaled breath condensate were significantly higher in the group of patients with pneumonia co-existing with lung cancer. In this simple manner the authors not only confirmed the systemic nature of acute inflammation observed locally in the lungs but also showed that other pathologies developing in the respiratory system have a fundamental effect on the reactivity of the immune system as a whole and on the reactivity of the local immune defences (as evidenced by the lower levels of proinflammatory mediators in peripheral blood in patients with pneumonia co-existing with lung cancer and higher in exhaled breath condensate). What is more, they very clearly demonstrated that local inflammation does not

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Received on 21 February 2011  
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 ISSN 0867–7077

develop into a systemic pathology merely as a result of simple “extension” from the affected area. As the study assessed only a limited number of inflammation markers, it could not establish whether the nature of inflammation in the lungs and that of inflammation in the peripheral blood were different and if so, how different. The study, however, clearly demonstrated that the intensity of local inflammation did not translate directly into its systemic activity.

Recognition of the fact that the respiratory system is an integral element of the human body and that pulmonary pathologies have significant extrapulmonary consequences necessitates searching for answers to a number of very specific and practical questions, such as questions about inflammation developing systemically and locally in the lungs. The study discussed above clearly demonstrates that the activity of both types of inflammation is not comparable. It is not known whether their nature, cell profile and cytokine profile are similar. The data available in the literature are insufficient to provide a unequivocal answer. It is, however, unlikely that these two processes could be identical. A simple example: in COPD patients, relative neutrophil counts in induced sputum are commonly elevated but usually normal in the peripheral blood. Both populations of cells are characterised by an altered biological activity evidenced by a significant increase in the formation of free oxygen radicals [3].

These deliberations cast doubt on whether inhalation anti-inflammatory treatment equally affects both processes. Are we modifying the systemic response when we target the local process? Or, conversely, can systemic treatment beneficially alter the activity of pathological processes in the respiratory system? A very interesting conclusion has been put forward in the clinical study by Szczegielniak et al. published in the present issue. They carried out a comprehensive respiratory physiotherapy programme in a group of patients with COPD assessing its effect on local inflammation in the airways by monitoring IL-8 levels in induced sputum [4]. Following three weeks of physiotherapy the levels of IL-8, a proinflammatory cytokine le-

ading to potent chemotaxis and activation of inflammatory cells, were considerably reduced in all the patients but particularly so in those with the highest baseline IL-8 levels in induced sputum. The authors confirmed therefore that rehabilitation was indeed a very important therapeutic tool from the clinical point of view in patients with COPD. They also showed that systemic interventions may significantly modify the activity of local inflammation.

While listing further concerns and practical implications resulting from the systemic effects of respiratory diseases it should also be recognised that an opposite situation might well be the case. It may well be that the respiratory disease is the main local manifestation of a generalised pathology. In some patients with COPD, symptoms of systemic inflammation are not observed, while in others systemic inflammation persists despite smoking cessation and a significant improvement of the clinical picture in the respiratory system [5].

In order to solve these dilemmas we require a more detailed knowledge of the mechanisms responsible for the close relationships that undoubtedly exist between systemic inflammation and local inflammation in the lungs. Elucidation of these mechanisms will not only allow us to successfully prevent extrapulmonary complications of lung diseases but also to treat patients more effectively.

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