Eur Respir J
1990, 3, 987–988

EDITORIAL

Oxidants and bronchial inflammatory processes

A.B. Tonnel, B. Wallaert

Oxidants are defined as any atom, group of atoms or molecule in which there is an unpaired electron in the outer orbital. Oxidants such as reactive oxygen intermediates (ROI), *i.e.* superoxide anion and hydrogen peroxide, are produced by phagocytes activated by either phagocytosis, biological or chemical stimuli [1]. Hence, an increased generation of ROI occurs during oxidant-dependent microbial killing processes and during inflammatory reactions, along with other bioactive mediators. In this context, several experimental studies support the hypothesis that an increased amount of oxidants may be responsible for lung inflammation and/or damage either directly (by peroxidation of membrane lipids and deoxyribreonucleic acid (DNA) damage), or indirectly (by inhibiting certain protein functions, especially α_1-proteinase inhibitor) [2]. This condition may result from injury to the lung by external agents that contain oxidants (such as cigarette smoke), that induced oxidant formation [3] or that are oxidants by themselves [4].

However, despite extensive clinical and laboratory investigations, there is no conclusive evidence that ROI generate by activated phagocytic cells may contribute to the development of bronchial inflammation. Indeed, the precise role of ROI in the pathophysiology of inflammatory processes remains unclear for the following reasons: 1) the evanescent nature of ROI accounts for the difficulty in the identification of ROI produced in the inflamed lung and bronchi; 2) ROI may be produced by several cell types, the activated state of which may be different; 3) the effects of ROI on cellular and non-cellular components depends on the antioxidant defence mechanisms *in situ*.

One of the most crucial problems is the identification and detection of the ROI involved since most of the reaction mechanisms turn out to be complicated and nonspecific. For example, determination of superoxide-dependent chemiluminescence is a rather popular assay. The yield of chemiluminescence depends upon the number and degree of activation of phagocytes and of the presence of substrates susceptible to oxidation yielding electronically excited products. To enhance chemiluminescence, the use of fluorescing sensitizers such as luminol, luciferin or lucigenin is usually considered as advantage. However, WARD *et al.* [5], in this issue of the Journal demonstrated that luminol and lucigenin amplified chemiluminescence by different mechanisms and different specificities for oxygen radical: luminol-amplified chemiluminescence exclusively reflects neutrophil (and eosinophil) activity whereas lucigenin-amplified chemiluminescence would appear to be an appropriate marker of alveolar macrophage activity when the proportion of polymorphonuclear cells is limited.

Therefore, another relevant major problem is to determine a cause and effect relationship between oxidant production and the development of an inflammatory reaction *in situ* and to demonstrate such effects *in vivo*. Although eosinophils are though to play a crucial role in asthma and bronchial hyperreactivity, there is clear evidence that blood eosinophils differ from tissue eosinophils. Several studies support the concept of heterogeneity of eosinophils in allergic asthma, as judged by the presence of a high percentage of blood low-density eosinophils [6]. Moreover, this impaired distribution of blood eosinophil subpopulations may be related to the clinical severity of asthma, supporting the hypothesis that biological assessment of blood cells is of interest in a better understanding of the pathophysiology of asthma. CHANEZ *et al.* [7], in this issue of the Journal, have reported that blood eosinophils from symptomatic patients with asthma exhibited an increased chemiluminescence response to exogenous stimuli when compared with eosinophils from asymptomatic asthmatic subjects. However, when activated by an immunoglobulin E (IgE) dependent stimulus, blood eosinophils induce the release of small amounts of platelet aggregating factor (PAF)-acether, a thousand times lower than do lung eosinophils [8]. Consequently, one may suspect that the observed aberrations of circulating inflammatory cells only suggest that these cells are "activated" (the mechanisms responsible remain to be elucidated), but do not necessarily infer that ROI generation plays a direct role in bronchial inflammatory processes.

At the bronchial level, using bronchoalveolar lavage, it was also demonstrated that stimulated alveolar macophages from patients with asthma generated significantly more ROI than alveolar macrophages from controls [9]. Several lines of evidence suggest a role for these cells in initiating and perpetuating bronchial inflammation but the precise role of ROI is not yet understood.

In testing the hypothesis that ROI are important in bronchial inflammation, it will be necessary to better define pharmacological strategies of antioxidant therapy

* Service de Pneumologie et Immuno-Allergologie, Hôpital A. Calmette and Institut Pasteur, Lille, France.

that might decrease oxidant-mediated injury without altering physiological processes that require oxidant generation. Since little is known about the role of oxidants in the immunoregulatory reactions and repair mechanisms, we have to be cautions in accusing ROI of the inflammatory crime until more convincing evidence of its guilt is demonstrated.

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