Pathogenesis of Chronic Lung Disease

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Chronic lung disease (CLD) of preterm infants has a multifactorial etiology. Pulmonary immaturity, oxygen toxicity and mechanical injury (barotrauma) as well as additional factors (hyperhydration, persistent ductus arteriosus, infection) may contribute to pulmonary damage. The mechanisms of acute lung injury are incompletely understood. There is growing evidence, however, that an inflammatory pulmonary reaction following lung injury may be an early event in the development of CLD, finally leading to lung fibrosis [1]. CLD is associated with a significant inflammatory response of the airways and the interstitium of the lungs. Besides neutrophils which are the predominant cells, macrophages immunoreactive for tumor necrosis factor- α are found in large number [2]. Neutrophil influx is possibly mediated by chemotactic factors present in the alveolar secretions. Leukotriene B₄, C₅a, interleukin-1, interleukin-8, elastin fragments and other factors may contribute to the high chemotactic activity [3]. Intercellular adhesion molecule-1, which has been detected in bronchoalveolar secretions of infants with CLD, may promote neutrophil diapedesis [4]. Furthermore, a number of lipid mediators including leukotrienes, prostacyclin and platelet-activating factor were found to be elevated in bronchoalveolar lavage fluid. These and other mediators exert various effects on the airways and the vascular system by increasing the micro-vascular permeability which is one of the most important pathophysiological factors of early CLD [1].

Neutrophils and macrophages attracted to the site of injured tissue can cause severe lung damage by release of potent proteases (elastase, collagenase) and generation of toxic oxygen radicals. The presence of free elastase activity and oxidative inactivation of α_1 -antitrypsin inhibitor which protects the alveolar-capillary unit from autolytic proteolysis has been well documented [5]. The protease-anti-protease imbalance as well as toxic oxygen radicals released by phagocytes or generated by tissue-bound xanthine oxidase may play a central role in lung injury [6]. In fact, increased concentrations of elastolytic fiber deg-

increased production and secretion of various cytokines, transforming growth factor and fibronectin by a number of cells may well contribute to pulmonary inflammation, tissue destruction and fibrotic repair [9].

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Extended Abstracts

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