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Airway wall remodeling in young and adult rats with experimentally provoked bronchial asthma

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Obstructive airway disorders represent one of the major health issues in industrialized countries. It is reported that approximately 40 % of the population is at increased risk of the allergy that can melt into bronchial asthma [1]. Morphological and immunological studies having documented the presence of an active inflammation in the airway mucosa have been gradually changing the opinion on this disease and its treatment. Together with the inflammation, various structural changes known as remodeling constantly appear in the bronchial walls of patients suffering from the bronchial asthma [2]. The principle of the remodeling mainly consists in changes of properties of the bronchial epithelium including hyperplasia of its goblet cells, thickening of the basement membrane predominantly in the area of its reticular lamina, differentiation and activation of myofibroblasts and proliferation of smooth muscle in the airway walls, growth of submucosal glands, deposition of extracellular proteins to the lamina propria mucosae and changes of vascularization [3]. While these morphological changes in bronchial walls of patients with asthma have been thoroughly described, predominantly in the adults, fewer papers exist about the bronchial remodeling in small children and even lesser about the changes in laboratory animals. The reason of this state is probably the fact that the spontaneous asthma practically does not occur in animals [4].

There is only one isolated paper describing differences in the remodeling changes in two age groups of animals that simulates the developing asthma in children [5]. This study showed the more pronounced airway remodeling at a young age. Thus, we decided to analyze structural changes of intrapulmonary airways in rats of Brown Norway (BN) strain, which are especially responsive to sensitization by various allergens and tend to develop the state that clinically and morphologically highly resembles the human bronchial asthma when stimulated with appropriate allergen challenges.

Young (4 weeks) and adult BN rats were sensitized by repeated intraperitoneal injections of ovalbumin (OA). During following 2 weeks, the rats regularly inhaled the aerosolized OA of low concentration. Two control groups of each age were housed simultaneously. The first of them was injected and inhaled by saline (S), the second group was untreated (C). At the end of the experiment, the animals were sacrificed, their lungs were processed for the light microscopy and the intrapulmonary airways were examined. In this study, we concentrated to the airway morphometric parameters, occurrence of eosinophilic granulocytes in the airway walls and number of epithelial secretory cells together with a glycoconjugate quality of their secretion.

The airway walls of the OA group were showing marks of remodeling in both young and adult animals. The total wall areas of all intrapulmonary airways were significantly increased compared to groups S and C (Figure 1). The thickening of inner wall areas (mucosal and muscular layer) was more pronounced in adult rats; outer wall areas (adventitia) were more increased in the young group. There were some significant signs of the muscular hypertrophy or hyperplasia only in young challenged animals (Figure 2). The number of eosinophilic granulocytes was predominantly increased in airway walls of OA young rats (Figure 3). The cells were found mainly in the tunica adventitia (Figure 5). Secretory cells were more multiplicated in airway epithelium of OA adult animals (Figure 4). Proportions of neutral and acidic glycoconjugates in their secretion were shifted towards the acidic ones in adult rats (Figure 6).

The study confirmed the bronchial sensitivity of BN rats and different reactivity of adult and young individuals. The remodeling changes were ascertained in all layers of the airway wall; more in the epithelium and connective tissue than in the muscle. A morphological base for further experiments was constituted. We expect significant changes in the extracellular matrix composition.

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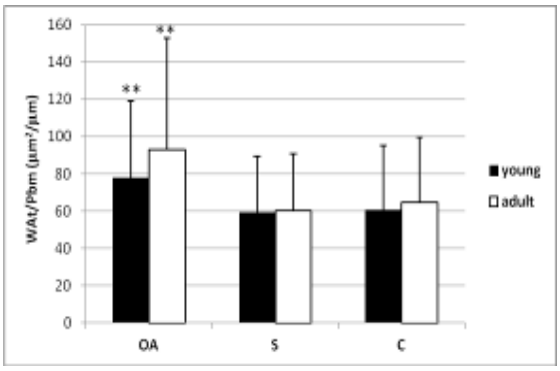

Figure 1. Total wall area (WAt) normalized to perimeter of basement membrane (Pbm) in all measured intrapulmonary airways.
** p < 0.01 versus S and C

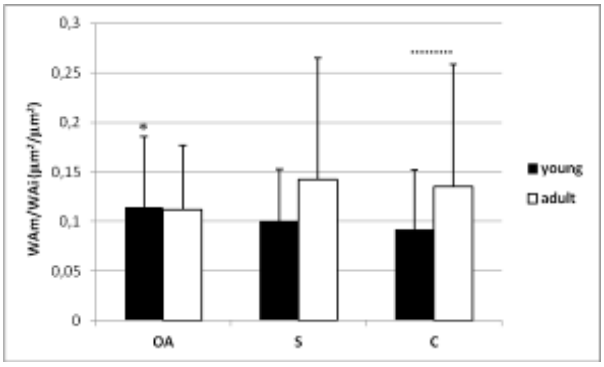

Figure 2. Area of smooth muscle (WAm) / inner wall area (WAi, mucosa and muscular layer) in all measured intrapulmonary airways.
* p < 0.05 versus C, dashed line p < 0.05

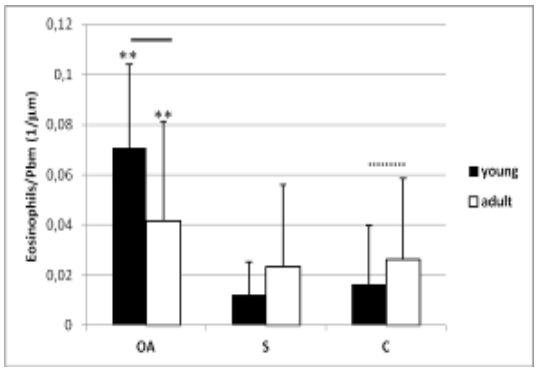

Figure 3. Number of eosinophilic granulocytes normalized to perimeter of basement membrane (Pbm) in all measured intrapulmonary airways.
** p < 0.01 versus S and C, solid line p < 0.01, dashed line p < 0.05

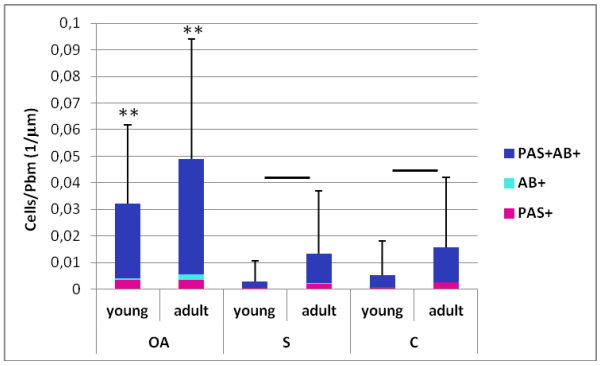

Figure 4. Number of epithelial secretory cells normalized to perimeter of basement membrane (Pbm) in all measured intrapulmonary airways. Proportions of PAS and/or alcian blue (AB) positive cells are showed.
** p < 0.01 versus S and C, solid line p < 0.01

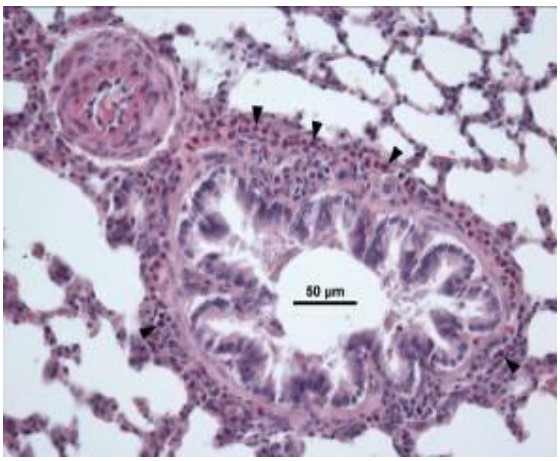

Figure 5. Small bronchiole of OA young rat. Many eosinophilic granulocytes (arrowheads) are present mainly in tunica adventitia. Hematoxylin and eosin staining, objective magnification 40x.

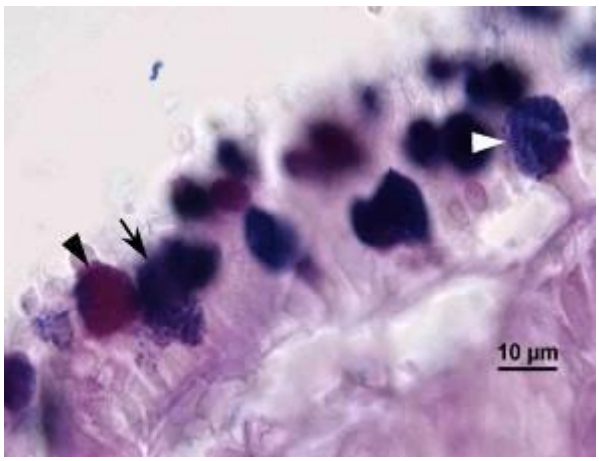

Figure 6. Secretory cells in bronchial epithelium of an OA adult rat. Glycoconjugates are visualized by PAS and alcian blue (AB), pH 2.5. All three histochemical reactions of secretory granules are visible: neutral PAS+ (black arrowhead), acidic AB+ (white arrowhead), combined PAS+AB+ (black arrow). Objective magnification 100x.