On November 14-15, 2008, the third Scandinavian COPD Research Symposium was held at Holmenkollen Park Hotel Rica, Oslo, Norway. Like the previous meetings, arranged 2004 (1) and in 2006 (2), the purpose was to let young scientists from our countries come together and present their current COPD-related research. The meeting should also facilitate collaboration and stimulate further research in the field of COPD. For the first time, Finland joined the symposium and eleven young scientists from Denmark Finland, Norway and Sweden presented their latest data and five State-of-the-Art lecturers covered two sessions. “Inflammation and structural changes in COPD” and “COPD – comorbidities”. The meeting was generously supported by grants from Boehringer-Ingelheim and Pfizer.


ABSTRACTS — STATE OF THE ART

Inflammation in COPD

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The role of inflammation in the pathogenesis of COPD has been emphasised during the last years, and this area is now intensively researched. The current concept of inflammation as a response to environmental noxious agents, as cigarette smoke resulting in a local airway inflammation is getting increasing evidence. However, recently systemic inflammation has been studied, where still the hen and egg debate between local and systemic effects is ongoing.

The local inflammation in the airway is involving innate and adaptive immune reactions. Throughout the airway inflammatory reactions are seen, most well studied in morphological samples of smokers with and without COPD. In most patients there is a central bronchitis seen, with inflammatory cells, hypertrophia of mucous producing cells and glands. In the bronchioles the inflammation can be intensive in spite of relatively mild COPD. Emphysema can occur early in the development of disease, and recently it has also been emphasised that there is often an intensive vascular inflammation in COPD lungs. Most inflammatory cells are recruited and activated in the airways of COPD patients. The epithelium as the first resort for noxious agents is activated, with certain pro-inflammatory activities. Macrophages are recruited to both the airway parenchyma and perhaps more important to the airway lumen, the obvious reason being phagocytosis particles in the cigarette smoke. They also take part in the further recruitment of inflammatory cells as neutrophils. Both macrophages and neutrophils produce proteases, with important effects on the alveolar structure during emphysema development. Both cell types also produce oxygen radicals, which further enhances the inflammatory reaction, and also decreases the antiprotease activity in the airway. Lymphocyte reactions seem to be abundant in the COPD inflammation, and the number of cytotoxic T-lymphocytes(CD8 positive) is well correlated to the severity of the disease, with early changes also in the preclinical phase. A more recent finding is that the adaptive immune system is involved...
in the formation of lymphocyte follicles in the lungs, more common in advanced disease, and dominated by B-lymphocytes. Cells more commonly described in asthma pathogenesis also seem to be involved in COPD. Eosinophils are more common in central airways biopsies in smokers than in non-smokers, and these cells are more commonly seen in the mucosa during COPD exacerbations. Mast cells have also been seen in central airways in smokers, and recently their occurrence in peripheral airways is under investigation.

The issue of systemic inflammation is also under intensive research currently, with certain emphasis on comorbid conditions in COPD. Of special interest is the coupling between COPD and cardiovascular disorders, mostly related to atherosclerosis. Very recent results from our group indicate that vulnerability for systemic inflammatory reactions could be a risk factor for the development of COPD, as elevation of acute phase proteins in subjects clearly increased the risk of being hospitalised decades after the measurement of the acute phase proteins (Engstrom G et al. Thorax 2009, e-publication).

The concept of inflammation in COPD is under development, and hopefully this knowledge will in the future increase the treatment possibilities in COPD.

Structural changes in COPD: Remodelling in COPD and asthma: differences and similarities

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Remodelling can be defined as alteration of tissue architecture. This dynamic process involves a number of cells including structural cells and occurs both during normal organ development and in response to injury. Chronic inflammation and remodelling are linked, and may result difficulties in maintaining normal tissue function. Diagnosis of asthma and COPD is based upon limitation of expiratory airflow. The pathophysiological correlates to this lung function impairment are complex but are associated with development of structural changes in the airways and lung parenchyma. In addition, the preceding inflammation differs, both between the two diseases, but also between various airway and lung compartments and may also differ from one patient to another. Both asthma and COPD are heterogeneous disorders including various phenotypes and there is a considerable overlap between the two diseases.

In asthma, airways obstruction is thought to be predominately located in the large airways. Thus, epithelial desquamation, subepithelial fibrosis and increased smooth muscle mass are seen and may, together with inflammatory infiltration lead to airway narrowing. Recent studies have, however, indicated that inflammation and probably also remodelling in asthma are also present in other compartments in the lung, such as the small airways.

In the large airways in COPD, there is an increased amount of goblet cells and glands which may result in the clinical picture of chronic bronchitis. However, the large airways are not the major site of the airways obstruction in COPD. Instead, structural changes in the small airways and lung parenchyma are the main correlates for the limitation of expiratory airflow. In the small airways, peribronchiolar fibrosis (bronchiolitis), are seen and the wall thickness in COPD have been found to correlate to forced expiratory volume in one second (FEV1). Bronchiolitis in COPD may be accompanied by emphysema, i.e. destruction of alveolar walls resulting in a decreased gas exchange area.

Thus, localization of the structural changes differs between the two diseases suggesting that they should be treated differently. Currently, the main pharmacological treatment of asthma and COPD are bronchodilators and glucocorticoids. It seems that the more distal in the lung the remodeling occur, the more irreversible it is to this available treatment.

In COPD and severe asthma, available pharmacotherapy has not proven to restore lung function impairment. It is therefore increasingly recognized that research aiming to explore mechanisms of airway remodeling should be encouraged. This may lead to development of new therapeutic strategies in order to interfere with the biology of structural cells, hopefully resulting in a possible restoration of lung architecture.

COPD — Comorbidities

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Chronic obstructive pulmonary disease (COPD) is defined by chronic airflow limitation associated with an abnormal pulmonary inflammatory response of the lungs to inhaled particles and gases, usually cigarette smoke. However, it is now recognised that in addition to the effects in the lungs COPD, like many chronic diseases has systemic consequences which result in comorbidities which influence both morbidity and mortality.

The cause of these systemic effects is not well understood but is thought to result from a systemic inflammatory response, which produces the systemic effects such as weight loss, muscle wasting, and increased risk of cardiovascular disease, metabolic syndrome, cancer and osteoporosis. The ageing process is characterised by progressive, generalised impairment of function resulting in an increasing vulnerability to environmental challenge and an increased risk of disease. Accelerated ageing is a further hypothesis which could account for both the local lung and systemic effects of COPD.

The diagnosis and assessment of severity of COPD may be greatly affected by the presence of co morbid conditions and it may be that in addition to lung function measurements, assessment of cardiovascular