THE PATHOPHYSIOLOGY OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

Giancarlo Folco

Center for Cardiopulmonary Pharmacology, Dept. of Pharmacological Sciences, School of Pharmacy, Univ. of Milan, Via Balzaretti 9, 20133 Milan, Italy
Email: giancarlo.folco@unimi.it

COPD is a complex human disease defined as "…a state characterized by airflow limitation that is not fully reversible…is usually both progressive and associated with an abnormal inflammatory response of the lungs to noxious particles or gases". The pathophysiology of COPD is complex, it cannot be attributed to a single cause and comprises mucociliary dysfunction, widespread airway inflammation and structural changes leading to expiratory flow limitations (EFL). COPD patients also present extrapulmonary, systemic manifestations, such as weight loss and cardiovascular disease that contribute at least partially to airflow limitation and overall reflect systemic inflammation.

Airflow limitation is a commonly recognized contributor to COPD with various underlying factors identified as playing a major role in the disease, such as contraction of smooth muscle, hyperreactivity and loss of elastic recoil. Distruction of the parenchymal support in the small airways may cause airway narrowing and loss of elasticity, leading to decreased EFL, inefficient CO_2 and O_2 transfer and lung hyperinflation.

Mucus hypersecretion is also a prominent feature of COPD and patients exhibit ciliary abnormalities, augmented viscosity of the mucus and less efficient mucociliary transport. Moreover, recurrent airway infections can cause additional airway damage and loss of ciliated cells, triggering a vicious cycle that further impairs mucus clearance.

The state of chronic inflammation that characterizes COPD is caused by recruitment and activation of an increased number of neutrophils, macrophages, mast cells and T lymphocytes (especially $CD8^+$) in various parts of the lung, which are driven by inflammatory mediators, particularly cytokines and chemokines. The tissue damage caused by the inflammatory cell infiltrate may then be amplified by other mechanisms such as oxidative stress and/or reduction of antioxidant capacity.

Chronic airway inflammation is also associated to repeated cycles of repair and damage that lead to remodelling of small airways and emphysema; mucous glands become enlarged, the epithelium undergoes squamous metaplasia and airway smooth muscle proliferation occurs. Muscle weakness and a reduction in muscle mass is commonly reported and the capacity of the respiratory muscles (e.g. diaphragm) is reduced.

In conclusion, COPD should be considered as a systemic disease with significant comorbidities that may contribute to its severity and mortality.