Asthma and smoker's lung: dry airways play a key role

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Dry airways may not only play a central role in the development of the inherited lung disease cystic fibrosis, but also in much more common acquired chronic lung diseases such as asthma and smoker's lung, the cigarette smoke-induced chronic obstructive pulmonary disease (COPD). This is the conclusion reached by scientists at Heidelberg University Hospital under the direction of Assistant Professor Dr. Marcus Mall from the Department of Pediatrics at Heidelberg University Hospital and Professor Dr. Richard Boucher of the University of North Carolina at Chapel Hill. In animal studies, they found that insufficient hydration of the airway surfaces leads to pathologies typical of chronic obstructive lung diseases in humans.

Thus, these findings point to a new approach for the treatment of these diseases, which are listed by the World Health Organization WHO as the fourth leading cause of death world-wide. There are currently no causal therapies available for treating these diseases; only the symptoms such as shortness of breath and oxygen deficiency can be treated. The results of the study have now been published in the "American Journal of Respiratory and Critical Care Medicine".

Cystic fibrosis gene causes airways to dry out and thickens mucus

In the hereditary disease cystic fibrosis, which affects about 8,000 people in Germany (about 80,000 people in the Western world), a defective gene causes a change in the transport of salt and water across the mucosal surfaces in the lungs, the intestine and other organs, and thus produce a change in the composition of the secretions.

Using a mouse model he developed, Dr. Mall succeeded in proving a direct relationship between the defective gene and development of lung disease – certain sodium channels on the surface of airway cells that are responsible for the resorption of salt and water are "hyperactive". The cells absorb too much fluid, causing the airway surfaces to dry out. This gives rise to thick "dry" mucus that cannot be cleared. As a consequence, the respiratory tract gets clogged with mucus – the lungs cannot be cleaned effectively of inhaled allergens, toxins and pathogens, giving rise to chronic pulmonary inflammation and respiratory insufficiency.

Dry airways lead to allergic inflammation, chronic bronchitis and emphysema

The research team from Heidelberg and the US has now for the first time studied the spontaneous course of lung disease caused by dehydration of airway surfaces in mice from birth to adulthood. "We found changes that are not only typical for cystic fibrosis, but also for other chronic obstructive lung diseases such as asthma, chronic bronchitis, and emphysema," reports Dr. Mall, head of the Heidelberg Cystic Fibrosis Center and also head of a research program funded by a Marie Curie Excellence Grant from the European Union.

In young mice, overly dry airways lead to allergic airway inflammation - characterized by an increase in specific white blood cells, the eosinophils - typically seen in asthma, a disease that affects every tenth child in Germany. Subsequently, adult mice gradually develop chronic bronchitis (dominated by neutrophils), and emphysema, i.e. the destruction of the small alveoli in the lungs that are responsible for the exchange of oxygen between air and blood. These changes are typical for lung disease caused by exposure to cigarette smoke.

Improved hydration through sodium channel blockers?

The researchers conclude that dehydrated airway surfaces could play a key role in the development of chronic obstructive pulmonary disease in

humans. These results indicate that improving hydration of airway surfaces and thus mucus clearance of the lungs, for example by blocking the sodium channels in the cells of the respiratory tract, could be a successful strategy for treating chronic obstructive pulmonary diseases of different etiologies. The Heidelberg research team now wants to test the benefits of this new therapeutic approach in animals.

Source: University Hospital Heidelberg