Editorial

Is there a link between lungs and gut? In bugs there is an answer
by Marco Confalonieri

Gastro-esophageal reflux is a classical example of a connection between the respiratory and the GI tracts. Pulmonary localizations of inflammatory bowel diseases and intestinal localization of pulmonary vasculitides are also well known as pathologies connecting the lungs and the gut. Generally speaking, to step outside of one’s field of speciality may allow to gather clues and gain insight into the roots of respiratory dysfunction. Some years ago, the GI specialist Talley (1) described how patients with asthma and allergic rhinitis may have abnormally high levels of eosinophils in both the airways and their intestines jointly with respiratory and GI symptoms. An even more challenging hypothesis was made by the research team led by Huffnagle (2) who claimed attention to the gut microbiota as a determinant of lung health. The researchers from the Michigan University intensely scrutinized the "lung-gut axis", the interplay of bugs in the gastro-intestinal tract with the respiratory system, and how it might influence chronic and acute pulmonary diseases. Thanks to the modern molecular analysis is possible a deeper scientific penetration of the microbiome than the traditional culture-based studies. Today, we know that the lungs are not sterile, as believed in the past, allowing the epiglottis a daily microaspiration from the pharynx, mainly during the night even in individual with perfectly normal swallowing function. Moreover, there is a growing awareness that...
the human microbiome is a seething ecosystem to be kept in balance with the immune system and the ambient microbiome interplaying a powerful role as genetics, lifestyle and environment in determining human health. The genetic material of the bacteria inside the human body outnumbers the human genes by a humbling factor of at least 200 to one, and for every bacterium there are not less than ten viruses. Differently from the intestinal tract, the movement of air, mucus, and microbes is bidirectional in the lung where the ambient is oxygen rich. Moreover, the vast majority of the lung alveoli surface area is lined with lipid-rich surfactant, which has bacteriostatic effects against select bacterial species. Thus, even if the lung microbiome is totally comparable with mouth microbiome, the bacterial density in the airways is quite modest, comparable to that of duodenum, and markedly different from the large intestine. Host-bacterial interactions are also different in lungs vs gut, the lungs exhibiting far more extraluminal interactions between bacteria and host immunity (alveolar macrophages). The relative reproduction rates of the different bacterial species hosted in the lung as determined by regional growth conditions and the immune system competence may change the lung microbiome, within an individual or across disease states, providing perturbation in the immunity-microbiome balance. The primary determinant of the lung microbiome in healthy subjects is the balance of bacteria immigration and elimination. However, during disease, the regional growth conditions change dramatically, creating permissive niches for selective bacterial reproduction. Chronic bronchopulmonary diseases during an acute exacerbation show a shift in the microbiome composition away from the bacteroides phylum, which dominates the healthy lung microbiome, towards proteobacteria, the phylum that contains many lung-associated gram-negative bacilli (3). Very recently, Huffnagle et al. (2) reported culture-independent evidence that the lung microbiome is enriched with gut bacteria in patients with ARDS. In patients with ARDS the bronchoalveolar lavage fluid shows commonly abundant gut-specific bacteria (Bacteroides spp) correlated with the intensity of systemic inflammation. These gut-specific bacteria are not detectable by traditional cultures and seem correlated more with systemic than alveolar inflammation. Thus, gut-lung bacteria translocation may be the mechanism correlated with systemic inflammation, whereas alveolar inflammation is correlated with disorders of the lung microbiome. Nevertheless, also transient immigration of gut bacteria has been demonstrated to alter the lung microbiome. Several trials showed that suppression of the gut microbiome is protective against multiorgan failure and mortality in patients with critical illness and culture identified translocation of gut bacteria to mesenteric lymphatics was already observed many years ago either experimentally and clinically. These recent findings open new perspective for the interpretation of the mechanism underlying pneumonia, particularly the most severe ones, and ARDS. Furthermore, we can now imagine novel potential therapeutic targets for the prevention and treatment of respiratory diseases with still a high mortality rate.

References