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Pulmonary vascular disease and infection: a tale of two diseases

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Pulmonary vascular disease (PVD) is a devastating condition affecting cardiac function and precipitating heart failure, and is associated with high morbidity and mortality rates. The progressive increase in pulmonary artery pressure (pulmonary arterial hypertension (PAH)) is the main haemodynamic manifestation of a complex of pathological changes in the vascular tree leading to right ventricular failure.

Whereas the pathogenesis of PAH is multifactorial, the final effect is vasoconstriction within the pulmonary circulation, which leads to an increase in pulmonary vascular resistance and pulmonary artery pressure. Indeed, changes in the main signalling pathways, i.e. the endothelin, nitric oxide and prostacyclin pathways, either alone or in combination, may contribute to an increase in pulmonary vascular tone, and to morphological changes ('remodelling') of the vascular wall that are difficult to reverse in those patients with a long history of PAH.

Inflammation holds a key position in the pathophysiology of pulmonary hypertension; however, there is still a considerable amount to be learned regarding potential stimuli and triggers of inflammation, including infectious agents. In the present issue, Pullamsetti *et al.* will give a better insight into the inducers/triggers of chronic inflammation and infection, and on the inflammatory mediators and cells that are involved in pulmonary hypertension.

The precise role of infectious diseases in the pathophysiology of PAH is under investigation, but PVD has been associated with various infectious diseases, such as human immunodeficiency virus (HIV) disease and schistosomiasis, and with other clinical conditions that are commonly associated with infectious agents, including chronic liver disease with portal hypertension, chronic obstructive pulmonary diseases, cystic fibrosis, and pulmonary interstitial diseases.

PVD associated with HIV infection represents a challenge for physicians dealing with HIV-infected patients. The introduction of potent antiretroviral treatment for HIV-infected individuals resulted in longer and better survival and lower mortality from opportunistic infections among this large population of patients that, according to UNAIDS, in 2008 accounted for 33.4 million people. However, the longer survival of HIV-infected patients has also drawn attention to some severe complications such as neoplasm, neurological diseases, and cardiovascular involvement. Most of the currently increased attention regarding cardiovascular involvement in the course of HIV infection has focused on the metabolic disorders caused by antiretrovirals and the subsequent risk of cardiovascular diseases. However, since the beginning of the AIDS epidemic, a severe cardiovascular–pulmonary disease has been observed, i.e. PAH that is clinically and histologically indistinguishable from the other forms of PAH. In their review, Cicalini *et al.* report the main epidemiological, clinical and therapeutic highlights and the new hypotheses on the pathogenesis of HIV-related PAH.

HIV infection is widespread in the world's population, but also other infections related to pulmonary hypertension, such as schistosomiasis, are also a concern, owing to their diffusion worldwide. Schistosomiasis (bilharzia) is the third leading endemic parasitic disease in the world, following malaria and amoebiasis. More than 200 million individuals are infected, and another 600 million are at risk of acquiring the infection. The disease is endemic in eastern South America, the Caribbean islands, East Asia and different areas of China and the Middle East; sub-Saharan Africa is the area with the highest endemicity. It is calculated that 2–5 million people worldwide develop PAH because of schistosomiasis. However, only few countries have managed to eradicate the infection or have undertaken successful and sustainable control programmes. *Schistosoma* worms live in the perivisceral veins of the intestine, liver and genitourinary systems, and have a life cycle that involves certain species of freshwater snails. The lung is a mandatory step in the parasite's life cycle. This causes both acute and chronic pulmonary lesions, depending on the cycle phase, as discussed in the review by Butrous *et al.*

Other infections have been more recently associated with PAH, and include pertussis, tuberculosis, human herpesvirus 8 infection, and filariasis and other helminthic diseases.

Pertussis is ranked among the ten leading causes of childhood mortality, and causes an estimated 254 000 paediatric deaths every year. The most catastrophic clinical complica-

tion of pertussis in infants is intractable pulmonary hypertension, leading to failure and shock, and currently recognized as a frequent problem in infants with fatal pertussis. In fact, pertussis should be suspected in any infant death associated with marked leukocytosis, bronchopneumonia, or refractory pulmonary hypertension, particularly in children aged <4 months.

Interestingly, the role of bacteria in the development of pulmonary hypertension could also be associated with their capacity to enhance fibrotic remodelling, as hypothesized following thrombosis in patients with chronic thromboembolic pulmonary hypertension, thus resulting in a misguided thrombus resolution. In these patients, thrombus infection appears to be a trigger in the evolution of chronic thromboembolic pulmonary hypertension.

There is a noticeable lack of awareness regarding the association of pulmonary hypertension with infectious diseases; the reviews in this issue will increase its understanding among specialists involved in the care of patients with infections.

Transparency Declaration

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