hyperdynamic state with low pulmonary vascular resistance and rapid microvascular transit, and 2) vascular remodelling with dilatation of capillaries and a low transfer factor of the lung for carbon monoxide. After liver transplantation, arterial oxygen tension improves, but transfer factor of the lung for carbon monoxide often remains low [5], implying improvement in process 1 more than process 2. Since pulmonary nitric oxide levels return to normal after orthotopic liver transplantation [6], nitric oxide is an unlikely cause of the pulmonary capillary dilatation. Figure 1 in the *European Respiratory Journal* editorial [2] focuses on pulmonary vascular smooth muscle, but it cannot be the only factor.

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DOI: 10.1183/09031936.04.00095604

*From the authors:*

Our recent editorial [1] argued that increased nitric oxide (NO) production is an important factor underlying the molecular mechanisms that cause pulmonary vascular dilatations in the hepatopulmonary syndrome (HPS). J.M.B. Hughes rightly points out that there is likely to be more to it than just the vasodilatory effects of NO to account for gross capillary dilatations typically found in the HPS. Indeed, there is little smooth muscle to relax in normal capillaries, and increased capillary diameters by a factor of 10 would be an unlikely consequence of vasorelaxation. We agree that other vasodilating mediators, such as carbon monoxide and the vasoactive intestinal peptide, along with an overexpression of the endothelin B receptor [2, 3], are likely to be involved in a complex reversal of angiogenesis at the pulmonary arterioles and capillary network [4, 5]. Capillaries and arterioles are not fixed structures, but are the net result of dynamic antagonistic processes of growth, repair, senescence and apoptosis. In HPS, this finely tuned balance would be disrupted in favour of dominant apoptosis and senescence, while pulmonary hypertension is the opposite situation of excessive uncontrolled angiogenesis. That the liver controls the constant remodelling of the pulmonary circulation is illustrated by the fact that pulmonary vascular dilatations occur when systemic veins are directly connected to the pulmonary circulation following surgical treatment of congenital heart defects [4–6]. These patients develop pulmonary vascular dilatations and pulmonary shunting, much like that observed in the HPS, and these abnormalities resolve after redirection of hepatic veins to the cavopulmonary connection [6].

J.M.B. Hughes also points out that after liver transplantation, pulmonary vascular resistance increases and arterial oxygen tension improves, but the carbon monoxide transfer factor remains low, suggesting a return to normal of arteriolar tone with restoration of pulmonary vasoreactivity to improve the matching of perfusion to ventilation, but persistently dilated pulmonary capillaries. Whether this is really the case remains uncertain. The carbon monoxide transfer factor cannot be anything but a very imperfect measure of pulmonary capillary calibre, and there are many causes of abnormally low carbon monoxide transfer factor in liver-transplanted patients. The pulmonary vascular dilatations after liver transplantation have been shown to reverse over time, although slowly and not always completely in the case of gross dilatations [4, 5, 7]. Here also, we agree with J.M.B. Hughes that a return to normal of endogenous nitric oxide production is unlikely to be the sole determinant of the reversal of pulmonary vascular structure and function to normal equilibrium state.

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DOI: 10.1183/09031936.04.00127604