ELEVATION OF REGIONAL PULMONARY resistance in response to local alveolar hypoxia is a near-universal response of the mammalian lung to optimize arterial oxygenation (14). Given the heterogeneity of regional ventilation observed in a normal lung (11, 16), it appears plausible that hypoxic vasoconstriction might act to fine-tune the precision of the match between local blood flow and ventilation. In a study in the Journal of Applied Physiology, Arai et al. (1) describe high-resolution MRI measurements of pulmonary blood flow in humans, comparing flow distributions with subjects breathing room air and 30% oxygen. Their finding, explored with four different statistical evaluations of their measurements, was that administration of 30% oxygen did not change pulmonary blood flow dispersion. Repeating the same measurements with subjects breathing 12.5% oxygen likewise failed to yield any significant change in flow distributions. These findings of the constancy of pulmonary blood flow distribution with hyperoxic and hypoxic interventions support the hypothesis that the spatial distribution of pulmonary blood flow is primarily determined by the anatomic configuration of the pulmonary artery tree. Previous studies in animals have demonstrated that the spatial distribution of weight-normalized pulmonary blood flow is only minimally influenced by changes in posture (4), microgravity (3), or potent pulmonary vasodilators (5, 13). Studies utilizing a computational model of pulmonary flow distribution based on high-resolution measurements of human pulmonary arterial tree anatomy, and incorporating the influence of different postures and gravity, also concluded that the vascular structure is the primary determinant of pulmonary blood flow distribution (2).

Arai et al. (1) describe their flow measurements normalized by tissue density, an important refinement of in vivo measurements that allows for appropriate comparison with the weight-normalized flow measurements described in animals. The original gravitationally directed perfusion gradients described in upright and supine lungs utilized methods that could only detect regional blood flow without correction for differences in lung tissue density (17). It is now clear that the weight and elastic properties of a blood-perfused lung mandate that the less dependent regions will be rarified by the weight of the dependent regions, a gravitational influence recently dubbed “the Slinky effect” (9). Using the same weight-normalized analysis described by Hopkins et al. (9), Arai et al. (1) report that both the dorsal and ventral thirds of the supine lung have equivalent but lower flows per gram of lung parenchyma relative to the midlung zones. These findings in humans are concordant with both the weight-normalized measurements made in animals and the computational model predictions based on human vascular anatomy (2). While recent high-resolution studies support the predominance of pulmonary vasculature anatomy in flow distribution, it is important to acknowledge that active debate continues to simmer on this issue (6, 10).

Do the findings of Arai et al. (1) establish that hypoxic vasoconstriction is not operative in a normal, normoxic human lung? Not necessarily, as there are limitations to both the measurement technique and the data analysis that could conceal a modest influence of hypoxic vasoconstriction. First, the MRI flow measurements reported here sample only a small portion of the lung. Although the overall extent of weight-normalized blood flow heterogeneity can be reliably estimated from limited sections of lung parenchyma (4), spatially defined regions of the lung can increase their flows in transition from normoxia to hyperoxia (7). It is possible that hyperoxia-responsive regions exist in human lungs but were not adequately sampled in the present study by the location of imaging planes. A second limitation is that the statistical analysis of the MRI data lacks the sensitivity to detect small changes, even though it had been adequate in a previous study to detect increases in blood flow heterogeneity after hypoxia in high-altitude pulmonary edema-susceptible humans (8). Given the large normal range of pulmonary blood flow heterogeneity, if only a few low-flow regions increased their perfusion in response to hyperoxia, that change could readily escape detection. A more sensitive test of the influence of hyperoxia on blood flow distribution would be to compare multiple small regions of interest in normoxia and hyperoxia. However, comparing small regions of flow images acquired at functional residual capacity at two different times in conscious humans would be technically challenging. A final limitation of the MRI flow measurements alone is that low-flow regions may have low, normal, or high ventilation-perfusion ratios (VA/Q), as the overall heterogeneity of ventilation is well matched to the heterogeneity of perfusion (15). A better test of whether hypoxic vasoconstriction functions in a normoxic human lung would be to determine whether low VA/Q units in a normal lung increase their perfusion in response to hyperoxia, but that test will require quantitative high-resolution measurements of both ventilation and blood flow.

Hyperoxia does alter regional blood flow distribution in sheep (12) and juvenile pigs (7). Both of the latter studies had regional ventilation and blood flow marked with fluorescent labels at each inspired O2 fraction (FIO2). Each lung piece sectioned after death contained VA/Q information at every FIO2, so that registration error was not an issue. Hlastala et al. (7) identified a spatial cluster of pieces in pig lungs that decreased blood flow when the FIO2 was reduced from 0.50 to 0.21, and that change in perfusion distribution was associated with a decrease in overall VA/Q heterogeneity. Hence, at least in pigs and sheep, it appears that an influence of hypoxic pulmonary vasoconstriction can be detected during normoxia. Whether
this difference in animal findings compared with the human findings of Arai et al. (1) is species specific or explained by differences in method sensitivity is unclear, but both factors could be operative.

Within the limits of their measurements and analysis, Arai et al. (1) have demonstrated that hypoxic vasoconstriction does not have an effect on human pulmonary blood flow distribution during normoxic breathing. This finding is consistent with the growing literature supporting the hypothesis that the anatomy of the pulmonary vasculature is the primary determinant of density-normalized blood flow distribution within the lung, and that the influences of vasoconstrictor, body position, and gravitational forces are minor by comparison. However, the findings of Arai et al. (1) do not exclude the possibility that a more sensitive analytic approach could show a measurable influence of hypoxic vasoconstriction in normoxic normal humans. One potential refinement would be the development of precise registration techniques for comparison of flow images acquired at different times. A yet more challenging goal to investigate the importance of hypoxic vasoconstriction in humans in normoxia would be the development of imaging methods to assess spatial VA/Q distributions at the same level of resolution now attainable with the current MRI blood flow measurements.

REFERENCES


