

Changes in pulmonary vascular responsiveness to hypoxia

We read with interest the recent article by Luks *et al.* (2017), which reports the relationship between arterial oxygen saturation and an echocardiographic index of pulmonary artery pressure (tricuspid transvalvular pressure gradient, TVPG) in healthy volunteers at sea level and after undertaking a two-week trek to Everest base camp. The authors report that, for each of the arterial oxygen saturations studied (range ~70-100%), pulmonary artery pressure was higher after around two weeks at altitude than it had been at sea level. They suggest that this finding might represent early pulmonary vascular remodelling, and cite two previous studies from our laboratory, in which TVPG does not return fully to baseline after an 8-h exposure to hypoxia, as evidence that this remodelling could start after even shorter periods of hypoxia. However, they note that since our studies did not include a control group, an alternative explanation for our findings is simple diurnal variation in pulmonary artery pressure.

We would like to make two points in relation to these previous studies, which may be of interest to readers of the article by Luks and colleagues. First, although we were indeed unable to exclude diurnal variation of pulmonary artery pressure in the specific studies cited, similar studies in our laboratory have identified no such variation. Balanos *et al.* (2005), for example, reported control measurements of TVPG every 1-2 h in a group of 8 healthy volunteers breathing air at sea level. Over the 12-h protocol, no significant changes in TVPG were observed, despite substantial diurnal changes in cardiac output over the same period.

Second, although we agree that structural remodelling is likely to contribute to the elevation of pulmonary artery pressure during prolonged exposure to hypoxia, we have previously interpreted the persistent elevation of TVPG following 8-h periods of hypoxia as a manifestation of enhanced pulmonary vascular sensitivity, rather than pulmonary vascular remodelling. In keeping with this conclusion, the pulmonary vascular response on re-exposure to acute hypoxia is substantially enhanced for at least 3 h following an 8-h exposure to hypoxia (Dorrington *et al.* 1997). In addition, we have previously reported that TVPG also fails to return immediately to baseline after exposure to just 105 min of isocapnic hypoxia (Talbot *et al.* 2005), a time frame over which structural remodelling seems very unlikely.

Finally, in contrast to the above findings in chamber studies at sea level, it is noteworthy that Luks *et al.* did not identify an increase in pulmonary vascular sensitivity to hypoxia after two weeks at high altitude. The explanation for this apparent discrepancy is not clear, but obvious methodological differences include the duration of exposure to hypoxia, and the presence of respiratory alkalosis at high altitude, which was prevented in our sea level experiments through dynamic end tidal forcing (Dorrington *et al.* 1997; Talbot *et al.* 2005). We have previously shown that respiratory alkalosis *per se* produces significant vasodilatation in the healthy pulmonary circulation (Balanos *et al.* 2003).

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Additional Information

Competing interests

None