Point:Counterpoint


REBUTTAL FROM HOPKINS, OLFERT, AND WAGNER

Our colleagues suggest that transpulmonary microbubble passage demonstrates shunting important for gas exchange during exercise (5). However, they themselves show that flow through vessels allowing 25 μm microsphere transmission is generally very small and have never demonstrated any associated gas exchange effect. They are trying to elevate the status of miniscule arteriovenous pathways into elephant-sized shunts.

They demonstrate microsphere transmission of only 0.001–0.05% of cardiac output at resting flows (6, 8), less than the small ~0.2% found with the multiple inert gas technique (MIGET). During exercise, MIGET-detected shunt in humans (3) and dogs (4) averages 0.1%. In exercising dogs (8), our colleagues report pulmonary microsphere transmission of 1.42%, which they interpret as a 1.42% shunt. In pulmonary gas exchange, shunt has only one definition—blood not exposed to ventilated alveoli during passage through the lungs. Shunted blood does not participate in gas exchange and arterial PO2 thus falls. Importantly in their dogs, PaO2 increased with exercise (from 99 to 106 Torr) while estimated AaDO2 was unchanged at 10 Torr. First, Pao2 increasing to 106 Torr contradicts the assertion that “shunts” are important during exercise. Second, a 10 Torr AaDO2 is entirely accounted for by a shunt of at most 0.6%. Thus the majority of the 1.42% flow indicated by microspheres cannot be a shunt. Third, if shunts appear only during exercise, why didn’t the AaDO2 increase during exercise?

Our colleagues find that microbubble transmission correlates with the AaDO2 during exercise (9), but many variables correlate without any cause-and-effect relationship. They also argue that precapillary gas exchange impairs the ability of MIGET to detect shunts, as low-solubility gases are eliminated upstream of shunt vessels. However, where pathologic intrapulmonary shunt and hypoxemia are expected (e.g., hepap-
topulmonary syndrome, pulmonary edema), shunt is readily detected with MIGET (1, 7). Also, since precapillary gas exchange has been shown for oxygen in normal lungs (2), their explanation is unlikely, as it should similarly overcome “shunting” for O$_2$ if such occurred in the arteriovenous pathways found by our colleagues.

Finally, they suggest that using 100% oxygen for measuring shunt is invalid, implying that O$_2$ constricts some of the pulmonary circulation (5). However what they demonstrate is the disappearance of microbubbles, not of shunt. There are several explanations for this that do not involve rewriting the textbooks on the effects of oxygen on the pulmonary circulation, including how changing gas partial pressures affect microbubble size (10).

REFERENCES


REBUTTAL FROM LOVERING, ELDRIDGE, AND STICKLAND

Our colleagues present several arguments why intrapulmonary shunts may be imaginary or if real, insignificantly small, like Horton’s Whos (4). They suggest that some saline bubbles are small enough to pass through capillaries. However, not all subjects shunt. If bubbles systematically squeezed through capillaries, it would occur in every subject (1, 10). More importantly, in the exercising dog nondeformable 25 μm microspheres traverse the pulmonary circulation during exercise (9). Since capillary distention even under extreme conditions appears limited to <15 μm (2), these microspheres are not squeezing through capillaries.

We agree the shunt flow is small in the isolated lung preparations; however, while the isolated lung studies approximated physiological conditions, they were not equivalent to exercise. This is supported by the observation that a 0.007% shunt is detected in isolated dog lungs but exercising dogs show a shunt of ~2% (9). Interestingly, a 2% shunt accounts for most of the gas exchange dysfunction not measured as V/Q abnormality by MIGET (5). Surprisingly, the authors highlighted work demonstrating no shunting in exercising horses as we have detailed previously the flaws with that study’s design (8).

Our colleagues suggest that gas exchange within vessels responsible for microbubble transmission may not be impaired. We would suggest that if subclinical/undetectable pulmonary edema of the ~0.2 μm interstitial space could be responsible for significant O$_2$ diffusion limitation during exercise, then O$_2$ diffusion could also be limited (if occurring at all) in a 25–50 μm vessel with a wall thickness estimated to be ~2 to 4 μm (7).

Why MIGET is unable to detect these shunts is a mystery. A possible explanation is non-cappillary inert gas exchange (5). More perplexing, however, is why MIGET has not identified intracardiac right-to-left shunting through a patent foramen ovale (PFO) considering a prevalence of ~25% (3). MIGET would not be able to distinguish between intracardiac and intrapulmonary shunting; however, it seems with all the subjects studied a few PFOs would have surfaced, as they have in our studies (1, 6, 10). Recently we showed that hyperoxia closes inductable intrapulmonary shunt pathways (6), which would explain why the 100% O$_2$ test also failed to identify these shunts.

Dr. Seuss said, “Sometimes the questions are complicated and the answers are simple.” The evidence of exercise-induced intrapulmonary shunt in simple: saline contrast bubbles and microspheres traverse the pulmonary circulation during exercise, but not at rest. Regardless of their size, like Horton’s Whos, the shunts are real, and likely important.

REFERENCES