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Transit of micro-bubbles through the pulmonary circulation of Thoroughbred horses during exercise

A. La Gerche [a,*], J.R. Daffy [b], D.J. Mooney [b], G. Forbes [c], A.J. Davie [d]

[a] St. Vincent's Department of Medicine, University of Melbourne, Fitzroy, Australia
[b] St. Vincent's Hospital, Fitzroy, Australia
[c] Faculty of Veterinary Science, University of Melbourne, Parkville, Australia
[d] Southern Cross University, Lismore, Australia

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ABSTRACT

It has been observed that microbubbles may pass through the pulmonary circulation of dogs and humans during exercise. In humans, this phenomenon has been associated with lower pulmonary artery pressures, enhanced right ventricular function and greater exercise capacity. In the exercising Thoroughbred horse, extraordinarily high cardiac outputs exert significant pulmonary vascular stresses. The aim of this study was to determine, using contrast echocardiography, whether Thoroughbred horses performing strenuous exercise developed pulmonary transit of agitated contrast microbubbles (PTAC). At rest, agitated contrast was observed in the right ventricle, but not in the left ventricle. However, post-exercise microbubbles were observed in the left ventricle, confirming the occurrence of PTAC with exercise but not at rest. Further investigation is warranted to investigate whether this phenomenon may be associated with superior physiology and performance measures as has been implicated in other species.

The classic understanding of the normal pulmonary circulation is that all of the blood leaving the right ventricle passes through the pulmonary microcirculation via capillaries before returning to the left side of the heart through the pulmonary venous circulation. However, recently investigators have used saline contrast echocardiography during exercise to demonstrate the pulmonary transit of agitated contrast (PTAC) in humans (Eldridge et al., 2004; La Gerche et al., 2010; Lalande et al., 2012; Stickland et al., 2004). Consistent with these findings, Stickland et al. demonstrated that microspheres bypassed the pulmonary microcirculation in exercising dogs (Stickland et al., 2007). The size of these agitated contrast or microsphere "bubbles" (typically 15–25 μm) exceed the diameter of the pulmonary capillaries (typically 10 μm), and so they do not typically pass through the pulmonary microcirculation at rest (Eldridge et al., 2004; La Gerche et al., 2010; Stickland et al., 2004). It has been proposed that exercise-induced PTAC is the result of an increase in vessel caliber; either due to distension of the existing microcirculation or due to by-pass of the pulmonary capillaries via arteriovenous shunts (La Gerche et al., 2010). Either scenario would explain the observed associations between PTAC and lower pulmonary vascular pressures, enhanced right ventricular function and augmentation of cardiac output in humans (La Gerche et al., 2010; Lalande et al., 2012). This has potential significance for Thoroughbred horses. PTAC may be a marker of favorable pulmonary vascular physiology, enabling higher cardiac outputs at lower pulmonary vascular pressures.

The aim of the project was to determinewhether PTAC occurs in Thoroughbred horses during exercise.

Three fit and sound adult Thoroughbred geldings (aged 4–5 years) were included in the study. All three geldings had raced, and had undergone a minimum of three months of race training in Cranbourne, Australia. This study was approved by the Ethics Committee for Animal Research of Southern Cross University.

All three geldings were trained extensively on a treadmill and so were accustomed to treadmill exercise. The experimental treadmill exercise trial consisted of a five minute warm-up: one minute walk; two minutes trot (3 m/s); and two minutes canter (5.5 m/s) at four degrees elevation; then followed by two minutes gallop (8–10 m/s) at six degrees. The horse was then brought to a standstill. Heart rate was monitored using a Polar heart rate monitor (Polar s810i, Finland).

Jugular vein catheters were placed under local anesthesia (2 ml of 2% lignocaine; Ilium Lignocaine 20, Troy Laboratories 107 Pt. Ltd., Smithfield, Australia).

Contrast echocardiography was performed before exercise and in the immediate post exercise period, while the horse was standing on the treadmill. Contrast echocardiography was used to detect PTAC and intra-cardiac shunting. Standard procedures were employed. Briefly, the agitated contrast solution was prepared by

* Corresponding author. Tel.: +61 39288 4423; fax: +61 39288 4422.
E-mail address: andre.LaGerche@svhm.org.au (A. La Gerche).

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mixing, succinylated gelatin (Gelofusine, Braun International) with room air (95:5 ratio). The solution was agitated between two syringes using a three-way stop-cock to form fine suspended microbubbles. Microbubbles formed in this manner have previously been documented to measure 21.2 ± 6.2 μm (La Gerche et al., 2010). This is generally larger than the pulmonary capillaries in Thoroughbred horses (West et al., 1993). A 5 ml bolus of agitated contrast solution was administered intravenously through the jugular vein catheter over one second at rest and then immediately following completion of the exercise trial. This is analogous to the methodology previously validated in humans (La Gerche et al., 2010). Concurrently, all four chambers of the heart were imaged by two dimensional echocardiography and images recorded. The presence of an intra-cardiac shunt was determined by the appearance of contrast in the left ventricle (LV) in less than four heart beats (cardiac cycles), while with PTAC, contrast appearance in the left ventricle occurs after at least four heart beats. The potential outcomes were: visible contrast in the right ventricle (RV) and no contrast in the LV (no PTAC), visible contrast in the LV at least four cardiac cycles after contrast was visualized in the RV (PTAC), or visible contrast in the LV less than four cardiac cycles after contrast was visualized in the RV (intra-cardiac shunt) (Cottin et al., 2004; Stickland et al., 2004).

The same trained operator (DJM) performed all echocardiograms. The echocardiographic images were acquired with a 1.5 MHz standard matrix array transducer (Vivid I Echocardiograph; GE, Horton Norway). All images were recorded at a depth of 30 cm. Two-dimensional right parasternal long axis four chamber images and left parasternal long axis left ventricular outflow images were recorded as described previously (Long et al., 1992).

Jugular venous blood samples were collected two minutes post exercise (after the echocardiograms were recorded) into tubes containing anticoagulant heparin. Blood samples were analyzed immediately for lactate using a portable analyzer (Lactate Pro; Akray, KDK, Japan).

All horses tolerated the treadmill exercise trial well. In the exercise trial maximum heart rate was 217 ± 8 beats per minute. Post exercise blood lactate was 12.2 ± 2.2 mmol/L. Echocardiographic images were successfully obtained in all three horses at rest and immediately post exercise. At rest, there were visible contrast microbubbles in the right ventricle and none in the left ventricle, either within, or after four cardiac cycles following injection of agitated contrast solution (Figs. 1 and 2). Thus, there was no evidence of intra-cardiac shunting or PTAC in any of the three horses at rest. In contrast, immediately post-exercise, PTAC was observed in each of the three horses and occurred after more than four cardiac cycles (Fig. 1). That is, there was no evidence of intra-cardiac shunting, but there was evidence of exercise-induced PTAC.

We have demonstrated the transit of microbubbles through the equine pulmonary circulation following strenuous exercise, but not at rest. This is in agreement with recent studies, using contrast echocardiography, in humans that have demonstrated that exer-

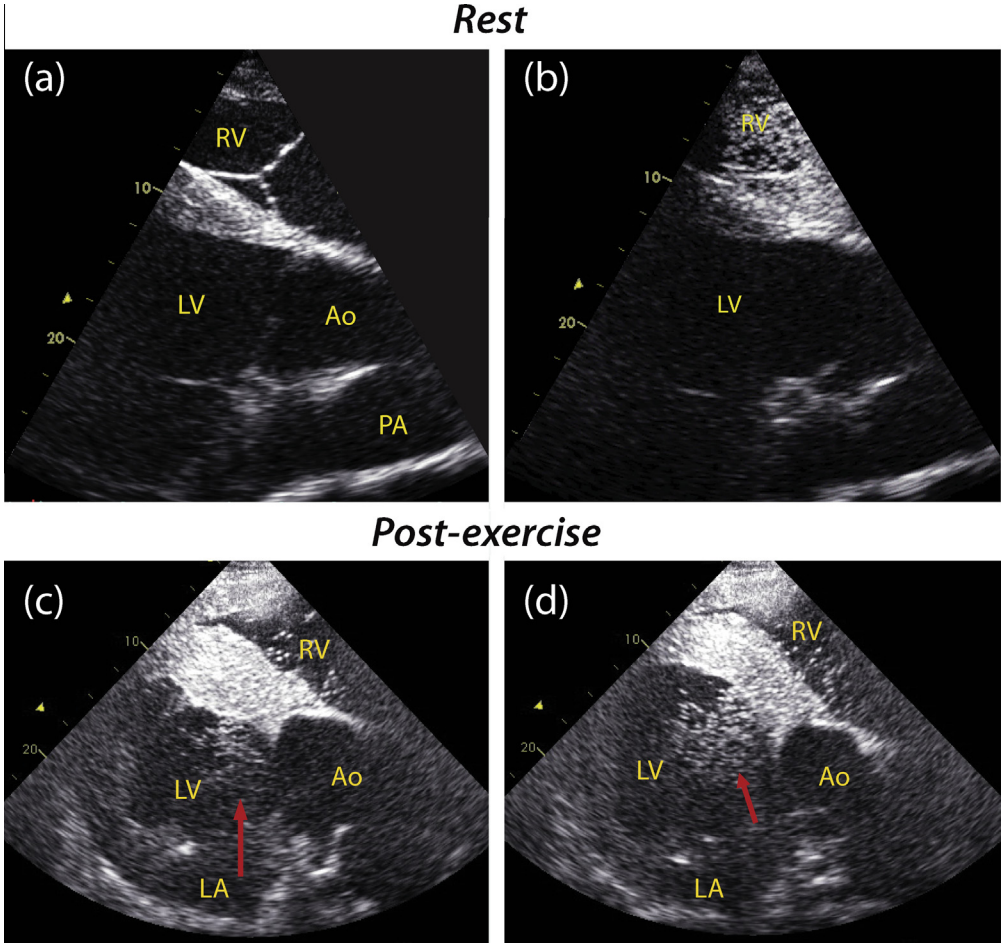

Fig. 1. Echocardiographic images depicting the presence of contrast in the left heart post-exercise but not at rest. A right-sided parasternal long axis four chamber view recorded at rest prior to contrast administration (a). Following contrast, microbubbles are observed filling the RV but no contrast is seen in the LA or LV (b). Immediately following exercise, sequential images (c and d) demonstrate microbubble contrast (identified with an arrow) passing from the LA across the mitral valve and into the LV. RV = right ventricle; LV = left ventricle; Ao = aorta; PA = pulmonary artery; LA = left atrium.