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Vascular pressures and passage of gas emboli through the pulmonary circulation

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Butler BD, Katz J. Vascular pressures and passage of gas emboli through the pulmonary circulation. Undersea Biomed Res 1988; 15(3):203–209.—Anesthetized dogs received venous air infusions at 0.35 ml · kg^{-1} · min^{-1}. In 60% of a group of 15 dogs, venous bubbles spilled over into the arterial circulation and were detected with the ultrasound Doppler technique. The pulmonary vascular pressure gradient (pulmonary artery pressure-pulmonary venous pressure or left atrial pressure) measured at the instant that spillover occurred was 34.7 ± 4.7 mmHg. In a 2nd group of dogs we raised the pulmonary vascular pressure gradient before the venous air infusions to achieve spillover of bubbles 100% of the time. The resultant pressure gradient at the time of spillover of venous bubbles was 52.0 ± 2.0 mmHg ($P < 0.05$). It is concluded that venous bubbles can cross the lungs of anesthetized dogs when the driving pressures are sufficient to overcome the normal filtering function.

air embolism
arterial bubbles
decompression
gas emboli
pulmonary vasculature
venous air embolism
Doppler

Venous air emboli (VAE) represent a constant threat to divers, aviators, and astronauts as an outcome of decompression-induced bubble formation. Whereas the most common type of decompression sickness (DCS) involves joint pain of a diffuse etiology, the presence of circulating venous bubbles are reported even in totally asymptomatic decompressions (1, 2). The more serious category of DCS (type II) includes cerebral air embolism that can result in permanent injury or death (3). The source of cerebral gas bubbles may be the result of bubble formation within systemic arteries, small airway rupture resulting in the injection of alveolar gas directly into the pulmonary veins, or venous bubbles that cross the pulmonary circulation (3–6). It has been demonstrated previously that VAE are normally filtered in the lungs (7–10) even when bubble diameters are as small as 21 μm. This includes bubbles in the size-range resulting from DCS (11). A limit to this filtration has been demonstrated experimentally when VAE were introduced at rates in excess of alveolar excretion (5, 6) resulting in arterial embolization. Brubakk et al. (12) also reported arterial gas

bubbles with ascending decompression excursions during He-O_2 saturation diving. The vascular route taken by the arterialized bubbles is uncertain.

For VAE to traverse a pulmonary vessel, the driving pressure pushing the gas bubbles must exceed the restrictive forces imposed by capillarity (13). It is well documented that VAE elevate pulmonary perfusion pressures and pulmonary vascular resistance (PVR). Investigators generally agree that mechanical obstruction of pulmonary vessels by the gas bubbles is an important factor in the elevation of pulmonary artery pressure (PAP) and PVR. Others have attributed these changes to neurogenic reflexes (14) or mediator release (15–17). These responses result in a redistribution of pulmonary blood flow to nonobstructed vessels (18). Therefore, the driving pressures that force venous bubbles through the lungs remain undefined. In the present study we have examined the pulmonary vascular pressure gradients in dogs receiving VAE where spillover of bubbles into the systemic arteries has occurred.

METHODS

Adult mongrel dogs (19 ± 7 kg) were anesthetized with pentobarbital sodium (30 mg/kg) and maintained with periodic doses of 5 mg/kg, intubated and ventilated with a Harvard respirator with 30% oxygen, balance nitrogen at a tidal volume of 13–17 ml/kg and a rate of 8–10 breaths/min. Baseline Pa_{CO_2} values were controlled at 35–40 mmHg. The left femoral artery and vein were cannulated for measurement of blood pressure (mean arterial pressure, MAP) and venous access. A left thoracotomy was performed between the 5th and 6th ribs for placement of a multi-lumen pulmonary artery catheter via the right jugular vein and manually directed so that the distal tip was located approximately 1 cm into the left lower lobe (LLL) pulmonary artery. A 7 Fr. silastic catheter was placed into the large LLL vein via the left atrium. A left atrial catheter was placed via the left atrial appendage for measurement of left atrial pressure (LAP). The catheters were connected to pressure transducers (Statham), referenced to the right atrial level and calibrated with a mercury column. Cardiac output was determined using thermodilution (Instrumentation Laboratories).

For detection of bubbles that crossed the lungs, a 9.5 mHz Doppler ultrasonic probe (Parks) was placed directly over the proximal portion of the descending aorta. After a 30–45-min stabilization period and collection of baseline data, room air was infused into the right atrium via the proximal lumen of the pulmonary artery catheter. The venous air was infused at 0.35 ml $\cdot$ kg^{-1} $\cdot$ min^{-1} using a reciprocating Servo pump (Harvard). This rate has been previously shown to cause spillover of venous bubbles into the arteries of dogs (6). At the instant that bubbles were detected by the Doppler, the pulmonary perfusion pressures were recorded. The driving pressure (ΔP) approximation was therefore determined as LLL PAP minus the LLL venous pressure (PVP), $\Delta P = PAP - PVP$.

In a 2nd group of dogs a Servo-controlled feedback system was used to control LLL PAP so as to elevate pulmonary perfusion pressure before infusing the VAE. These techniques, described in detail by Drake et al. (19, 20) enable the controlled diversion of pulmonary blood flow from the right lung into the LLL. Six dogs were anesthetized as previously described and ventilated with 100% oxygen. A left thoracotomy was performed and the 5th rib and left upper pulmonary lobes were removed. A 7 Fr. Fogarty balloon-tipped catheter was inserted into the upper left lobe artery

and directed into the right pulmonary artery. The catheter was sutured in place so that the balloon would remain properly located in the right pulmonary artery when completely inflated. A second catheter (double lumen) was directed into the LLL artery via the middle left lobe artery to measure PAP and infuse the VAE. Another catheter was placed directly into the left atrium via the left atrial appendage. In this series of experiments a second Doppler probe was placed directly over the LLL vein to detect bubbles crossing the left lung.

The Fogarty catheter was connected to a Servo control device consisting of a stepper motor drive that advanced or withdrew a saline-filled syringe to inflate or deflate the balloon (Fig. 1). The balloon was located in the right pulmonary artery in such a way that with complete inflation the blood flow to the right lung was diverted into the LLL. The Servo controller was operated by a comparator that matched the desired pressure in the LLL with the actual pressure measured from the LLL catheter. Therefore, to achieve maximum LLL pressure, the balloon was inflated to a point where blood flow to the right lung was minimal. Complete inflation of the Fogarty balloon was limited to less than 1 min to maintain blood gas values within the physiologic range. Using this technique, LLL arterial pressures were raised to values greater than 40 mmHg before the infusion of VAE as previously described. At the instant that pulmonary venous bubbles were detected by the Doppler, the

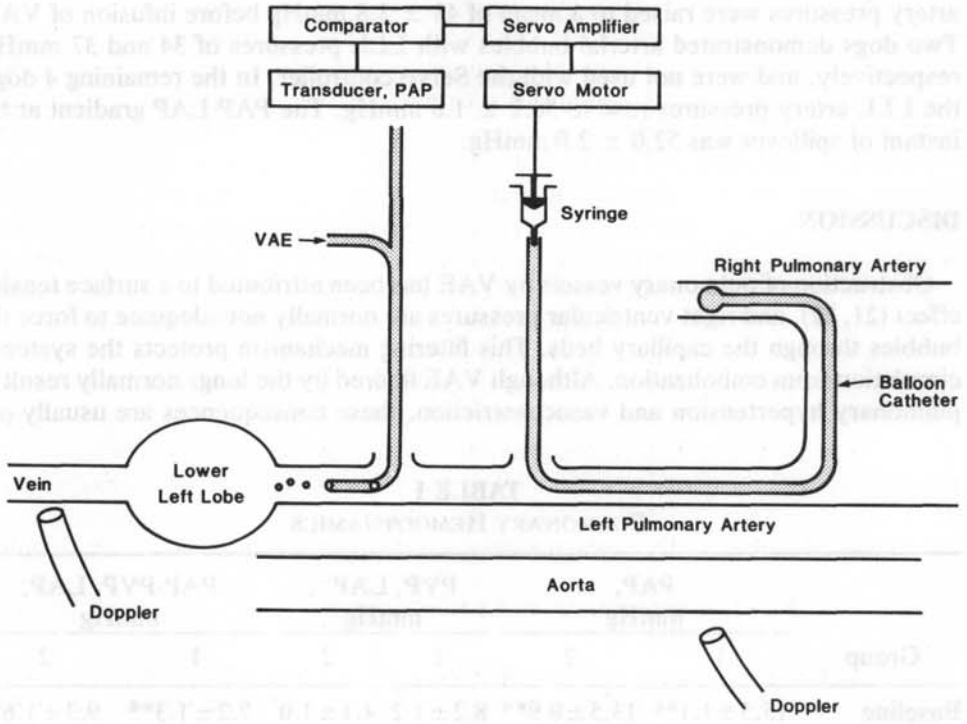

Fig. 1. Diagram of the surgical preparation for the 2nd group of dogs using the Servo-controlled feedback system to control LLL artery pressure before infusing the venous bubbles. LLL artery pressures were transduced for input into a comparator. The Servo motor-syringe controlled the degree of balloon inflation in the right pulmonary artery to divert blood flow into the LLL. Doppler probes placed over the aorta and LLL vein detected bubbles that crossed the lung.

pulmonary perfusion pressures (PAP-LAP) were recorded. Pressures were recorded from 12 embolizations in 4 dogs. At the conclusion of the experiments the animals were killed with KCl and the hearts were examined for the presence of septal defects.

Data in Table 1 were analyzed with using Student's *t* test with Bonferroni correction.

RESULTS

Pulmonary hemodynamic responses to the VAE are presented in Table 1. In the 1st group of dogs PAP increased 2.5-fold and PVR increased 6-fold following the VAE ($P < 0.05$). Left atrial and pulmonary venous pressures decreased following VAE, although these changes did not reach statistical significance. The PAP-PVP gradient increased from 7.2 ± 1.3 to 34.7 ± 4.7 mmHg ($P < 0.05$). The mean time (± SD) at which spillover of VAE occurred from the beginning of the air infusions was 7.4 ± 4.5 min. This corresponded to a mean (± SD) volume of 55 ± 36 ml of venous air. Airway pressures were unchanged with the VAE. Pulmonary venous pressures and LAP were 6.4 ± 1.7 and 5.9 ± 1.4 mmHg, respectively, at the instant of spillover. These data were collected from 10 dogs that had spillover of VAE into the arteries. Five dogs failed to demonstrate arterial bubbles. No animals had myocardial septal defects.

In the 2nd series of experiments using the Servo-controlled feedback system, LLL artery pressures were raised to a mean of 43 ± 3.8 mmHg before infusion of VAE. Two dogs demonstrated arterial bubbles with LLL pressures of 34 and 37 mmHg, respectively, and were not used with the Servo controller. In the remaining 4 dogs, the LLL artery pressures rose to 56.2 ± 1.8 mmHg. The PAP-LAP gradient at the instant of spillover was 52.0 ± 2.0 mmHg.

DISCUSSION

Obstruction of pulmonary vessels by VAE has been attributed to a surface tension effect (21, 22), and right ventricular pressures are normally not adequate to force the bubbles through the capillary beds. This filtering mechanism protects the systemic circulation from embolization. Although VAE filtered by the lungs normally result in pulmonary hypertension and vasoconstriction, these consequences are usually not

TABLE 1
PULMONARY HEMODYNAMICS

	PAP, mmHg		PVP, LAP⁺, mmHg		PAP-PVP, LAP, mmHg	
Group	1	2	1	2	1	2
Baseline	15.5±1.1**	13.5±0.9**	8.2±1.2	4.1±1.0	7.2±1.3**	9.3±1.6**
Air embolism	39.6±3.9*	56.2±1.8	6.3±1.2	4.1±0.8	34.7±4.7*	52.0±2.0

Data are means ± SE. *$P < 0.05$ compared to corresponding value in 2. **$P < 0.05$ compared to corresponding value with air embolism. ⁺PVP was not collected for group 2 dogs, LAP values are given for 2.

fatal and recovery is rapid (5, 6, 9). It is probably this ability of the lungs to filter VAE that accounts for the absence of symptoms in routine decompressions, even when venous bubbles are detected (2). If, on the other hand, VAE cross the pulmonary barrier, coronary or cerebral vascular obstruction can occur leading to permanent injury or death (3).

For VAE to spillover into the arteries, the driving pressures must exceed the forces of capillarity that tend to allow the bubbles to obstruct flow. This is described in the following relation (13):

$$\Delta P = 2\gamma \cos \theta / r \qquad (1)$$

where ΔP is the driving pressure gradient across the bubble (ΔP approximation = PAP-PVP or PAP-LAP), γ is surface tension, θ is the contact angle of the meniscus, and r is radius.

The results of this study indicate that the driving pressures forcing venous bubbles through the lungs were 34.7 ± 4.7 mmHg and 52.0 ± 2.0 mmHg. Substituting these values for ΔP into Eq. *1* and assuming that under static conditions the contact angle approaches (or is) 0° ($\cos \theta = 1$) and using a surface tension value of 50 dyn/cm, then the radii of the vessels that must be exceeded for bubbles to cross the lungs range from 17.2 to 29.2 μm (25.8 ± 6.1) for dogs in group 1 and 11.3 to 16.5 μm (14.4 ± 1.6) for the dogs in group 2. This coincides with the conclusions of Chang et al. (23) who determined that venous bubbles were trapped in vessels with diameters of 15–30 μm. From this it could be concluded that spillover of VAE into the arteries is via large capillaries or small arteriovenous pulmonary shunts (5, 24, 25), depending on the driving pressure gradient. The development of a contact angle (γ) (26) or a reduction in surface tension (γ) would further reduce the minimum diameter of vessel through which VAE could cross the lungs.

Previous investigators (7–10) have concluded that pulmonary vascular filtration of VAE is complete if relatively normal perfusion pressures are maintained. Others (5, 6, 27) have suggested that with larger volumes of VAE, spillover of bubbles is possible but an elevation in pulmonary artery pressure is required. Chang et al. (23) described the scenario whereby venous bubbles can traverse several generations of vessel branching until the driving pressures are inadequate for further advancement. With further dissolution of the gas in the bubble or changes in surface tension (28), the ΔP may then become sufficient to overcome the capillarity resistance. It is therefore likely that with greater volumes of VAE and hence greater driving pressures, the diameters of bubbles capable of crossing the lungs may also increase. Furthermore, with gas plug formation (21) bubble diameters may actually decrease with little or no change in volume.

The actual mechanism by which venous bubbles spill over into the arteries probably involves many interactions, both physical and chemical. Alterations in arterial carbon dioxide and oxygen tensions are reported with VAE (29) and their effects on pulmonary vessel diameter can influence the ability of the lungs to filter the bubbles. Further, vasoactive mediator release (15) or reflex changes in vessel tone (14) may be associated with VAE. Verstappen et al. (27) reported that VAE are excreted via the alveoli at rates proportional to PAP. With DCS it has been repeatedly demonstrated that venous and hence pulmonary bubbles usually precede arterial bubbles (30, 31). Thus, it is possible that with increased rates of VAE infusion or with extremely high PAP values, the dynamics of filtration as described above are over-

come and alveolar excretion cannot keep pace, allowing for systemic embolization. Pulmonary vascular pressure gradients demonstrated in this study suggest two sizes of derived vessel radii (25.8 ± 6.1 and 14.4 ± 1.6 μm) through which VAE may cross the lungs.

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Butler BD, Katz J. Pressions vasculaires et passage d'embolie gazeuse dans la circulation pulmonaire. Undersea Biomed Res 1988; 15(3): 203–209.—Des chiens anesthésiés (n = 15) reçurent des infusions veineuses d'air au taux de 0.35 ml · kg^{-1} · min^{-1}. Les bulles veineuses débordèrent dans la circulation artérielle et furent détectées avec la technique à ultrason Doppler chez 10 chiens (60%). Le gradient de pression vasculaire pulmonaire (pression artérielle pulmonaire—pression veineuse pulmonaire ou pression auriculaire gauche) mesuré au moment du débordement était de 34.7 ± 4.7 mmHg. Dans un deuxième groupe de chiens, le gradient de pression vasculare pulmonaire fut augmenté avant les infusions veineuses d'air afin d'obtenir un débordement de bulles dans 100% des cas. Le gradient de pression résultant au moment du débordement des bulles veineuses fut de 52.0 ± 2.0 mmHg ($P < 0.05$). Il est conclu que les bulles veineuses peuvent traverser les poumons chez les chiens anesthésiés lorsque la puissance des pressions est suffisante pour surmonter la fonction normale de filtration.

Butler BD, Katz J. Presiones vasculares y paso de embolo gaseoso a través de la circulación pulmonar. Undersea Biomed Res 1988; 15(3):203–209—Se aplicó a perros anestesiados infusiones venosas de aire a 0.35 ml · kg^{-1} · min^{-1}. En 15 perros (60%), las burbujas pasaron de la circulación venosa a la arterial, detectándose mediante la técnica de ultrasonido Doppler. El gradiente de presión vascular pulmonar (presión arteria pulmonar-presión venosa pulmonar o presión de la aurícula izquierda) medida en el momento del paso de las burbujas de la circulación venosa a la arterial, fue de 34.7 ± 4.7 mmHg. En el segundo grupo de perros, se aumentó el gradiente de presión vascular pulmonar antes de la infusión venosa de aire, para lograr el paso de burbujas en el 100% de las veces. El gradiente de presión durante el paso de las burbujas fue de 52.0 ± 2.0 mmHg ($P < 0.05$). Se concluye que las burbujas en el lecho venoso pueden atravesar los pulmones de perros anestesiados cuando las presiones que se ejercen son suficientes como para sobrepasar sus funciones de filtración normales.

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