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Venous air embolism: Clinical and experimental considerations

STEVEN L. OREBAUGH, MD

Objective: To examine the existing literature concerning venous air embolism. Causes, pathophysiology, and management are emphasized.

Data Sources: The literature that was reviewed was retrieved from the MEDLINE System under the headings "venous air embolism," "air embolism," "therapy of air embolism," "etiology of venous air embolism," and "pathophysiology of venous air embolism" for the years 1970 to 1991. A manual search, derived from the references of these papers, was performed to obtain relevant citations for the years preceding 1970.

Study Selection: Experimental (animal) data, case reports, case series, and clinical investigations are included.

Conclusions: Venous air embolism is an infrequent complication of invasive diagnostic and therapeutic maneuvers. The cardiovascular, pulmonary, and central nervous systems may all be affected, with severity ranging from no symptoms to immediate cardiovascular collapse. Therapeutic interventions include mechanical measures, such as positioning, withdrawal of air from the right atrium, and measures aimed at reducing bubble size. Hyperbaric oxygen therapy holds some promise in accomplishing the latter, but randomized, controlled trials demonstrating efficacy have yet to be performed. (Crit Care Med 1992; 20:1169–1177)

KEY WORDS: air embolism, venous; catheters, central venous; pressure, intrathoracic; invasive procedures; dyspnea; complications, iatrogenic; catheter, pulmonary artery; air embolus, paradoxical; air embolism, cerebral; hyperbaric oxygen

Venous air embolism is an infrequent occurrence that may be an iatrogenic complication of invasive procedures or may result from accidental trauma. Signs and symptoms vary from nonexistent to complete cardiovascular collapse, depending on the amount and rate of air entry. This review focuses on the pathophysiologic consequences and clinical manifestations of venous air embolism, appropriate therapeutic interventions, and the importance of preventive measures.

Etiology and Occurrence. Admission of air into the venous system may occur if several conditions exist: a source of gas (usually the atmosphere), a communication between the venous system and this source, and a pressure gradient favoring ingress of the gas. In the most direct example (1), air can be injected through a catheter into a peripheral vein or infused inadvertently via an improperly vented iv administration set, although this occurrence is infrequently reported. Likewise, air can enter the thoracic veins directly during central catheter insertion or during use after placement, due to the potential for subatmospheric intrathoracic venous pressure (2–14). Venous air embolism has been reported in penetrating chest trauma in humans (15) and in animals (16), and during surgical procedures involving lung parenchyma (17), as well as with bronchopulmonary venous fistulas caused by blunt chest trauma (18).

Neurosurgical and head/neck surgical procedures in the sitting position, and insufflation of air or other gases into the peritoneum, are other settings in which venous air embolism frequently has been described (19–22). Durant et al. (23) reported the occurrence of air embolism in the setting of maxillary sinus lavage, pneumothorax, and pneumoperitoneum. In total hip arthroplasty, venous air embolism is more frequent than previously thought, and is a probable cause of hemodynamic disturbances that formerly were attributed to methylmethacrylate cement (24–26). Use of the neodymium yttrium-argon-garnet laser in uterine surgery

From the Departments of Emergency Medicine and Clinical Investigation, Naval Hospital, San Diego, CA.

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Address requests for reprints to: LCDR S.L. Orebaugh, MC, USNR, c/o Clinical Investigation Department, Naval Hospital, San Diego, CA 92134-5000.

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has resulted in several deaths attributed to air embolism, as the instillation of air, CO_2, or nitrogen gas at high flow rates is required to cool the sapphire tip during the procedures (27). Positive-pressure ventilation in infants with hyaline membrane disease, and high peak airway pressure in mechanically ventilated adults both have been reported to cause venous air embolism (28–30). Vaginal insufflation during orogenital sex in pregnancy has also resulted in venous air embolism (31, 32).

The true occurrence of venous air embolism is uncertain, as this entity may be obscured by resultant cardiovascular, pulmonary, or neurologic manifestations that are felt to be primary in nature (33). If autopsy examination is delayed, air in the venous system or capillaries may be resorbed, contributing to the difficulty in diagnosis (21). In the operating room, where constant monitoring is done in high-risk patients, the occurrence rate of venous air embolism in neurosurgery or head/neck surgery when the patient is in the seated position is reported to be 21% to 40% (33).

Venous Air Embolism in Central Venous Catheterization. In the ICU, venous air embolism is most likely to be encountered during or after insertion of a central venous catheter. The occurrence rate of this problem is variable, reported from one in 47 central venous catheter insertions (34) to none in 355 (35, 36). Feliciano et al. (14) noted two cases in their report of >1500 subclavian vein catheterizations; James and Myers (10) reported only one case, a fatality, in 3,000 attempts at supraclavicular subclavian catheter insertion. The mortality rate of venous air embolism is significant: by 1987, a total of 79 cases had appeared in the world literature, and 25 (32%) of these cases had had a fatal outcome (3).

Since normally protective extrathoracic venous valves are transgressed when a central venous catheter is inserted, free communication may develop between the intrathoracic vasculature and the atmosphere. Admission of air then occurs whenever iv pressure decreases below ambient air pressure (33). Negative intrathoracic venous pressure is most likely to occur with deep inspiration, dyspnea, or hypovolemia, and in the upright position (5). During strained respiration, thoracic vein pressure may decrease 25 mm Hg below atmospheric pressure (21).

Numerous case reports (2–14) of venous air embolism related to central venous catheter insertion or use exist in the medical and surgical literature. Air may enter the great veins directly after the needle is inserted, if the hub is not conscientiously occluded (2, 4, 5, 14). However, the majority of cases occur not with the insertion of the catheter, but during use or maintenance of the catheter (2). Catheter hub fracture or disconnection has been associated with 63% to 93% of episodes of venous air embolism related to central venous catheters (5). Even a tract that forms during the use of a catheter-through-the-needle device, or a tract that remains after removal of a long-indwelling catheter can lead to venous air embolism (37, 38). Gas sequestered in the pleural space has been described as a source of embolism with subclavian vein catheterization (39).

Pulmonary artery catheter introducers have been implicated as causes of venous air embolism as well. Soon after the development of pulmonary artery catheters, anesthesiologists noted a potential for air embolism through introducers that were left in place for iv access after removal of the catheter (34, 40, 41). However, changes made by manufacturers followed, and self-sealing valves in introducers became standard (38). Some (40) suggested that valves in introducers might malfunction after being violated by pulmonary artery catheters, but *in vitro* studies (42) of four common brands failed to demonstrate airleaks in the unused state or after 48 hrs of cannulation by a catheter. Nevertheless, it is recommended that the introducer be removed along with the pulmonary artery catheter, or that an obturator be used to occlude the introducer if left in situ (40). Pulmonary artery catheters have been reported to cause venous air embolism related to pulmonary artery rupture after balloon inflation (43).

Pathophysiology. The alterations in cardiovascular and pulmonary physiology, resulting from admission of air into the venous system, have been well studied in animals. In 1947, Durant and colleagues (23) reported that the most important factors in determining mortality after experimental venous air embolism in dogs were: a) the amount of air entering the veins, b) the speed with which it enters, and c) the position of the body at the moment of embolization. Adornato et al. (44) distinguished between the cardiovascular effects of bolus venous air embolism and the effects of slow air infusion as can occur with a break in an iv line. With a bolus, the authors (44) noted an increase in central venous pressure, a decrease in pulmonary artery pressure, ST-segment depression on the electrocardiogram, and shock. These changes were thought to be due to an "air lock" in the right heart that was obstructing outflow. Slow, continuous infusion of air yielded an increase in central venous pressure and abrupt increase in pulmonary arterial pressure, decreases in systemic vascular resistance and mean arterial pressure (MAP), and a compensatory increase in cardiac output. Thus, the basic disturbance of cardiovascular function in venous air embolism is obstruction to right ventricular ejection. This disturbance may be at the pulmonary outflow tract, as in bolus air embolism, or at the level of

the pulmonary arterioles, as seen with slower infusions (21). Small bubbles lodge in pulmonary arterioles and create mechanical obstruction to flow, causing pulmonary arterial hypertension (7, 33, 45). Pulmonary vasoconstriction, demonstrated by Berglund and colleagues (46) in a canine model subjected to a slow air infusion, results in further compromise of right heart function. Durant et al. (23) reported rapid right ventricular dilation with evidence of ischemia after injection of an air bolus in dogs.

Similar effects are evident in humans. Bedford and co-workers (47) evaluated 100 seated patients during neurosurgical procedures with invasive hemodynamic monitoring and precordial Doppler ultrasound, and they detected 80 episodes of air embolism. Of these patients, 36 demonstrated increased pulmonary artery pressure, of whom a minority became hypotensive. Only those patients with an increase in pulmonary arterial pressure developed a decrease in MAP. A correlation was noted between the severity of hypotension and the degree of increase of pulmonary arterial pressure (47). Others (48) reported increased pulmonary arterial pressure in venous air embolism in humans as well. Venous air embolus occurring during surgery on the right side of the heart, resulting in postoperative pulmonary hypertension, has also been described (45).

Adornato et al. (44) found that air infusion rates of >1.8 mL/kg/min were fatal in dogs. They reported that a bolus of air >200 mL rapidly injected caused ventricular tachycardia and death in these animals. They (44) concluded that amount of air and speed of infusion are important factors affecting the mortality rate of venous air embolism (23). The lethal volume decreases as the rate of air entry increases. In humans, the fatal dose is uncertain, but estimates vary between 300 and 500 mL of air at 100 mL/sec (7). Such flow rates are attainable through a 14-gauge needle, if a pressure gradient of 5 cm H_2O exists (8). Lower volumes may prove lethal to the critically ill patient with compromised hemodynamics.

Microbubbles introduced into the pulmonary circulation result in significant ultrastructural changes and abnormalities of lung extravascular water content (49–51). The bubbles themselves obstruct flow and increase pulmonary arterial pressures; on the bubbles' surfaces, a network of fibrin, platelets, RBCs, and fat globules is constructed, which serves to further restrict blood flow (33). In sheep, Albertine et al. (51) demonstrated that neutrophils clumped around small bubbles in pulmonary arterioles are attached to the endothelium of these vessels. Ultrastructural changes included gaps between endothelial cells and disruption of the underlying basal lamina. This disruption produced an increase in lung lymph flow and protein flux, which was also demonstrated after infusion of 300-μm-diameter bubbles in sheep by Ohkuda et al (52).

The role of the neutrophil in lung damage produced by venous air embolism was further emphasized by Flick et al. (53), who demonstrated a greater increase in lung lymphatic flow after air infusion in sheep with normal numbers of circulating leukocytes, as compared with those sheep that had been rendered leukopenic. Jerome and colleagues (54) demonstrated protection from an increase in lung lymph flow and granulocytes in lung lymph when methylprednisolone was given before or during venous air embolism. Flick and coinvestigators (55) pursued the nature of lung microvascular injury by pretreating a sheep model of venous air embolism with heparin and superoxide dismutase. The characteristic increase in lung lymph flow and lymph protein content observed with venous air embolism was effectively prevented. The investigators (55) concluded that the superoxide anion, probably produced by leukocytes, plays an important role in the pulmonary microvascular damage of air embolism. In a related study (56), Flick et al. pretreated sheep subjected to air embolism with 50 mg/kg of iv catalase, which also prevented the expected effects of venous air embolism on lung lymph flow and protein content, supporting a role for the hydrogen peroxide molecule in the mechanism of pulmonary injury in this setting.

These histopathologic and cellular changes led to prominent abnormalities of pulmonary function. Lung compliance is reduced as a result of increased permeability and increased interstitial edema, and airway resistance is thereby increased (33). Hlastala et al. (57), using the inert gas elimination technique, demonstrated abnormalities of pulmonary ventilation-perfusion matching with resultant increases in physiologic dead-space and physiologic shunting. These aberrations underlie the hypoxemia universally found in victims of clinically important venous air embolism, both human and animal.

Natural History of Cardiovascular and Pulmonary Alterations in Venous Air Embolism. The natural history of venous air embolism has been described in animal models (23, 46, 50, 57). Adornato et al. (44) noted the changes in vital signs and venous pressures that occur with both graded venous air infusion and bolus introduction of air. In air infusion, the central venous pressure, the right pulmonary arterial pressure, and the heart rate all increased in a dose-related fashion, with air infusion rates of $\geq$ 0.4 mL/kg/min. At rates of >1.5 mL/kg/min, bradycardia supervened and cardiovascular decompensation began. No significant change occurred in BP until a rate of 1.7 mL/kg/min had been reached; thereafter, BP decreased rapidly. When

canines were subjected to iv boluses of air, the central venous pressure and heart rate again increased linearly with the dose of air, while BP predictably decreased in a dose-related manner. No change occurred in pulmonary arterial pressures until a dose of >100 mL of air was given. A 200-mL dose resulted in a coarse "mill-wheel" heart murmur and the death of the animal. In an investigation (58) of the hemodynamic effects of venous air embolism in sheep, a 60-mL air bolus rapidly caused a significant decrease in cardiac output in the majority of subjects within 1 min, while recovery to normal values was evident by 10 mins. The alterations in ventilation-perfusion matching demonstrated by Hlastala et al. (57), resulting from gas bubble infusion into canines, returned to normal 30 mins after the pulmonary insult. Presson et al. (49) described the effect of venous air emboli in dogs by directly observing the pulmonary circulation with an *in vitro* microscopy technique while air was being infused into the animals. Microbubbles were observed to lodge in the pulmonary arterioles and underwent spontaneous resorption after 60 to 180 secs. Larger doses of air seem to take longer to resolve. In a canine study (58), air bubbles persisted in the pulmonary circulation for 17.8 mins after an air bolus of 2 mL/kg when infused at 2 mL/sec. Butler et al. (59) demonstrated that pulmonary vascular bubbles remained for a mean of 26.9 mins.

Systemic Embolism Resulting From Venous Air Embolism. Venous air emboli may also result in air reaching the systemic circulation (60, 61). This phenomenon is referred to as "paradoxical" air embolism and usually occurs in the setting of a patent foramen ovale (61). While disturbances of cardiopulmonary physiology may be profound with air embolus confined to the right heart or pulmonary circulation, the consequences of systemic embolization are even more severe. Even small amounts of air can produce end-organ ischemia and infarction: as little as 0.05 mL of air injected into a coronary artery may cause focal infarction (62). Air emboli to the cerebral circulation frequently result in focal neurologic deficits (60).

Clinical Manifestations. Venous air embolism is variable in its clinical expression, both in its severity and in the organ systems affected. In canines (44) and in humans (63), a "gasp" has been reported to follow the initial infusion of air into the pulmonary circulation, possibly a reflex response. Intrathoracic pressure is then decreased, facilitating greater air entry. Patients often complain of breathlessness, light-headedness, chest pain, or a feeling of impending death (4, 7, 33). In one series of 14 cases, 100% of patients had sudden onset of dyspnea (64).

Signs that reflect the severity of air embolism are seldom specific for this entity. Significant emboli result in tachypnea, tachycardia, and frequently, hypotension. The only sign specific for air embolism, the rare "mill-wheel" murmur, is dependent on the presence of a large bolus of air in the right ventricle (21, 38, 63). A harsh systolic murmur (65) or normal heart sounds are more commonly found on examination. In a large proportion of patients, neurologic signs predominate. Kashuk and Penn (66) described a predominance of central nervous system manifestations in 42% of 24 instances of venous air embolism reviewed. These manifestations included altered mental status, frank coma, and focal deficits. Uncertainty exists as to whether hypoxia, hypotension, paradoxical embolism, or some combination of these factors are responsible for this neurologic compromise (4).

Minutes to hours after air embolism occurs, rales or wheezing can be detected on auscultation of the lung fields, evidence of pulmonary edema (66). In animal models (53–56, 67–69), the coexistence of increased pulmonary arterial pressure and pulmonary edema protein content with normal pulmonary artery occlusion pressures suggests that increased vascular permeability underlies the development of abnormal extravascular lung water.

Laboratory abnormalities also vary with the severity of the embolism, and lack specificity for this process. Electrocardiographic changes evident in canines include peaking of the P-wave and ST segment depression (23, 44). Reports in humans emphasize sinus tachycardia, nonspecific ST-segment and T-wave changes (13), and evidence of acute right heart strain (38, 70). Chest radiographs are usually normal initially, but later radiographs may show evidence of noncardiogenic pulmonary edema (67–69). An air fluid level in the central pulmonary artery or ventricle is rarely seen (6). Arterial blood gases reflect abnormalities of matching of ventilation and perfusion, usually as hypoxia, which may be profound (71). Hypercarbia is occasionally seen.

When utilized, invasive hemodynamic monitoring provides further evidence of clinically important air embolus. Increases in central venous pressure and pulmonary artery pressure are dose-dependent in animals subjected to slow air infusion (44). However, pulmonary arterial pressure may remain normal with an increased central venous pressure, presumably due to a large air bubble trapped in the right ventricle or pulmonary outflow tract. This phenomenon occurs in animals with massive air embolism (>5 mL/kg) (48). Of 40 cases of venous air embolism occurring during neurosurgery in the seated position in patients monitored with central venous catheters, 25% had an increase of central venous pressure (65). In a similar population of 100 patients monitored with precordial Doppler,

pulmonary artery catheters, and end-tidal P_{CO_2} equipment, Bedford et al. (47) described the occurrence of 80 cases of venous air embolism detected by Doppler, of which nearly half developed an increased pulmonary arterial pressure.

The utility of end-tidal P_{CO_2} monitoring to detect clinically important venous air embolism is well described (20, 21, 72). In the above-noted study of Bedford et al. (47), 30 of the 80 patients with venous air embolism reportedly had a decrease in end-tidal P_{CO_2}, reflecting disordered ventilation-perfusion matching and increased physiologic deadspace. Other useful indicators of venous air embolism include aspiration of air or foam from an indwelling central venous catheter or pulmonary artery catheter (48), and ultrasonography. Both Doppler ultrasound and precordial echocardiography are sensitive in the detection of intraoperative air embolism (71). However, only transesophageal echocardiography has proven useful in documenting paradoxical air embolism (73). Finally, Matjasko et al. (74) investigated end-tidal nitrogen monitoring for venous air embolism in canines and found that end-tidal nitrogen pathologically increases before the decrease in end-tidal P_{CO_2} in bolus embolism.

Differential Diagnosis. Venous air embolism may occur with a wide variety of signs and symptoms, and runs a continuum of severity from clinically insignificant to life-threatening, allowing an extensive differential diagnosis. When respiratory complaints and signs are primarily manifest, venous air embolism must be differentiated from other causes of sudden pulmonary compromise, such as pulmonary thromboembolism, pneumothorax, acute bronchospasm, and acute pulmonary edema. When no obvious predisposing factors or specific signs for venous air embolism are present to guide the clinician toward this diagnosis, consideration should be given to performing pulmonary angiography (or ventilation-perfusion scanning) to distinguish air embolism from thromboembolism, particularly in patients at high risk for the latter. If signs of central nervous system embarrassment predominate, the clinician must consider focal or global brain ischemia, hemorrhage into the parenchyma or subarachnoid spaces, hypoxia, trauma, and metabolic causes of rapid central nervous system deterioration such as hypoglycemia.

In many cases, cardiovascular compromise dominates the clinical picture. Usually, this situation takes the form of hypotension, in which case, venous air embolism must be considered, along with other causes of obstructive shock, hypovolemia, primary cardiac dysfunction, and acute vasodilatory states such as septic shock. Venous air embolism has also been reported (43, 75) to manifest as electromechanical dissociation, a potential result of right ventricular outflow obstruction, reducing the cardiac output without initially disturbing cardiac electrical activity. Therefore, one should consider this entity in the differential diagnosis of electromechanical dissociation when the patient is at risk for venous air embolism.

Management of Venous Air Embolism. Identification of the source of air entry and immediate measures to counter this entry are the first priority in the treatment of venous air embolism. Subsequent management strategies are based on evidence derived from animal investigations and case series in humans. Five areas of therapeutic intervention are discussed in the following sections: patient positioning, closed-chest cardiac massage, removal of air from the venous circulation, attenuation of bubble size, and miscellaneous measures not yet thoroughly investigated but with some promise in alleviating the effects of air embolism.

Patient Positioning. Durant et al. (23), in their early work with air embolism in animals, demonstrated increased tolerance by dogs to air infusion when the animal was lying on the left side, and improvement in hemodynamics of a compromised animal when turned onto the left side. On the basis of observations in open-chest animals, they (23) concluded that the left lateral decubitus position placed the right ventricular outflow tract in a position inferior to the right ventricular cavity, so that an air bolus would migrate superiorly, removing the obstruction to blood flow. Placing the patient with suspected venous air embolism in this position remains a cornerstone of management today (64, 76). The head-down or Trendelenburg position is recommended as well, apparently with similar effects on the position of the offending "air lock" in the right ventricle (7).

Closed-Chest Cardiac Massage. Closed-chest cardiac massage has been recommended as a means to force air out of the pulmonary outflow tract and into small pulmonary vessels, as it was successfully used by Ericsson et al. (77) in the resuscitation of four of five patients sustaining venous air embolism during neurosurgical procedures. External cardiac massage has been evaluated in canines as therapy for venous air embolism (76) and was found to improve survival rate as effectively as use of the left lateral decubitus position or aspiration of air from the venous system.

Removal of Air From the Venous Circulation. A more direct approach to the treatment of air embolism is withdrawal of air from the right heart. In 1956, Stallworth et al. (78) reported a case of cardiac arrest from venous air embolism occurring in the operating room. The patient was treated with percutaneous needle aspiration of 15 mL of air from the right ventricle, resulting in prompt hemodynamic improvement. More

recent reports have focused on removal of intracardiac air via central venous catheters. In canines, Adornato et al. (44) demonstrated a "dramatic reversal of shock with aspiration of air from the atrium." A study (76) comparing intracardiac aspiration from the right ventricle to external cardiac massage and to the left lateral decubitus position in treatment of venous air embolism in dogs resulted in similar survival in all three groups but significantly more rapid resuscitation with air aspiration than mechanical measures. Colley and Artru (79) found that a greater proportion of injected air could be removed from the right atrium of dogs with venous air embolism using a multiple-orifice central venous catheter than by either a 7-Fr pulmonary artery catheter or single port central venous catheter, resulting in significantly improved survival rate.

Data in humans are less promising. Michenfelder et al. (65) evaluated right atrial catheters in 23 episodes of venous air embolism in upright patients undergoing neurosurgical procedures. Significant air retrieval with a favorable influence on resuscitation occurred in only eight cases. In the series by Bedford et al. (47) of 100 patients undergoing seated neurosurgical procedures, 80 episodes of venous air embolism were detected by Doppler, but recovery of air from the pulmonary artery and the right atrium was minimal, only 2 to 20 mL. The authors concluded: a) recovery of air was not a major factor in improving hemodynamics, and b) packing the site of air entry with sponges and discontinuing nitrous oxide were more efficacious. Thus, withdrawal of air from the right atrium or ventricle is useful in venous air embolism if a catheter is present, but it does not justify the time and effort necessary to insert a central venous catheter in the acute situation if not already in place.

The optimal position of a right atrial catheter for recovery of air in venous air embolism was evaluated by Bunegin and co-workers (80), who utilized a Silastic model of the right atrium with pumps, infusing normal saline to evaluate fluid and gas interactions. Maximum recovery of air was achieved when the multiorifice catheter tip lay 2.0 cm distal to the junction of the mock superior vena cava and atrial chamber at an inclination of 80° from the horizontal.

Attenuation of Bubble Size. To reduce the size of embolized bubbles, all patients with suspected venous air embolism should be placed on 100% oxygen (33), as this approach favors nitrogen diffusion out of the bubbles and into the alveoli (nitrogen "washout"). For patients under anesthesia, it is imperative that nitrous oxide be discontinued, as it diffuses rapidly into all air-containing cavities in the body, including bubbles, significantly increasing their size and the obstruction they present to the circulation (81).

For those patients not responding to these measures, hyperbaric oxygen therapy should be considered. While well-controlled, randomized trials comparing this therapy with standard measures have not been conducted, many physicians advocate hyperbaric oxygen use on the strength of numerous case reports (82–88), reflecting clinical improvement in cerebral air embolism of venous or arterial origin after hyperbaric oxygen therapy. This modality has long been used in the therapy of arterial gas emboli resulting from decompression sickness in divers (89), but only more recently has hyperbaric oxygen therapy been applied to cerebral injury related to air embolism from therapeutic misadventures (84). Murphy et al. (60) reported a case series of 16 victims of cerebral air embolism from a variety of causes with signs of central nervous system dysfunction in which hyperbaric oxygen therapy was used. Fifty percent of the patients had complete resolution of signs of cerebral air embolism, while 31% had partial improvement. A delay in therapy of >5 hrs reduced the likelihood of improvement. However, complete resolution of neurologic signs and symptoms after air embolism has been reported with hyperbaric oxygen therapy for patients brought to therapy ≤29 hrs after the initial insult (32). While most studies in humans focused on improvements in neurologic manifestations of venous air embolism with hyperbaric oxygen therapy, Baskin and Wozniak (84) reported reversal of all cardiopulmonary abnormalities in seven of nine patients who sustained venous air embolism from hemodialysis, with more gradual resolution in the other two patients.

Hyperbaric oxygen may benefit patients with air embolism in several ways: a) descent to six atmospheres of pressure significantly reduces bubble size and relieves obstruction to blood flow; b) the extremely high Pao_2 and arterial oxygen saturation of hemoglobin that are achieved improve oxygen delivery to tissues that are partially ischemic; and c) high alveolar Po_2 favors nitrogen diffusion from bubbles in the pulmonary circulation into the alveoli, again reducing bubble size (83, 86). Thus, hyperbaric oxygen may improve hemodynamic compromise from right ventricular or pulmonary arteriolar obstruction, as well as reduce end-organ ischemia.

Hyperbaric oxygen therapy must be carried out under the direction of a physician experienced and knowledgeable in this area. Despite the anecdotal evidence cited, recent doubt has been expressed (90) concerning the efficacy of hyperbaric oxygen in cerebral air embolism; scientifically valid data are needed in this area.

Miscellaneous Measures. Several measures reported to be useful in the therapy of venous air embolism have

not yet been adopted in the treatment of humans. Tuman et al. (91) evaluated the protective effects of a perfluorocarbon emulsion as pretreatment in a canine model of venous air embolism. Dogs so treated sustained less of a decrease in cardiac index, left ventricular stroke work index, and MAP than the untreated controls, as well as significantly less hypoxia and hypercarbia. Studies in different animal models (92, 93) also demonstrated protective effects of fluorocarbon emulsions in air embolism. Cardiopulmonary bypass has also been advocated in the therapy of venous air embolism to ameliorate right heart strain (14). However, this therapeutic modality has not been systematically evaluated and its utility remains dubious.

Prophylaxis. Most episodes of venous air embolism are related to central venous catheters, making preventive measures particularly important when these catheters are inserted, used, or removed. The patient to undergo catheterization of the central veins should be placed in Trendelenburg position, which increases the central venous pressure and reduces the likelihood of air entry through the needle or catheter (4, 33). After entering the vein, and before insertion of the guidewire during use of the Seldinger technique, one should occlude the needle hub, releasing the obstruction to insert the wire only after asking the patient to perform the Valsalva maneuver, or time the insertion of the wire to coincide with exhalation (5, 82). Ellermeyer and Keifer (94) developed a through-the-plunger guidewire system that may reduce the risk of air embolus.

Ensuring adequate hydration before catheter insertion also mitigates against the low venous pressures that will permit air entry (78). All connections to the central venous line should be tightly sealed using Luer-Lok connections (4). Placing an occlusive dressing over the catheter when in place, and over the tract for 24 hrs after removal, will also help prevent air emboli (5). As with insertion, removal of the catheter in a head-down position is recommended.

In the operating room, monitoring for air embolism during high-risk procedures with precordial Doppler and end-tidal P_{CO_2} monitoring has become standard (33). Gas insufflation for diagnostic purposes should be accomplished with CO_2, not air, as the former has a low surface tension and causes less obstruction if embolism occurs.

Finally, if a patient experiencing air embolism can be ventilated with positive pressure, this procedure is preferable to spontaneous ventilation, as it reduces unfavorable pressure gradients permitting air entry. However, high peak inspiratory pressure causing barotrauma may, in itself, be a cause of venous air embolism and must be avoided (29).

REFERENCES

1. Yeakel AE: Lethal air embolism from a plastic blood storage container. *JAMA* 1968; 204:175–177
2. Borja A: Current status of infraclavicular subclavian vein catheterization. *Ann Thorac Surg* 1972; 13:615–622
3. Seidelin PH, Thompson AM: Central venous catheterization and fatal air embolism. *Br J Hosp Med* 1987; 25:438–439
4. Putterman C: Central venous catheterization. *Acute Care* 1986; 12:219–234
5. Peters SG: Mediastinal air-fluid level and respiratory failure. *Chest* 1988; 94:1063–1064
6. Gibson RN, Hennessy OF, Collier N, et al: Major complications of central venous catheterization. *Clin Radiol* 1985; 36:205–208
7. Lambert MJ: Air embolism in central venous catheterization. *South Med J* 1982; 75:1189–1191
8. Ordway CB: Air embolus via CVP catheter without positive pressure. *Ann Surg* 1974; 179:479–481
9. Peters JL, Bradford R, Gelister JK: Air embolism. *Intensive Care Med* 1984; 10:261–262
10. James PM, Myers RT: Central venous pressure monitoring. *Ann Surg* 1972; 175:693–701
11. Puri VK, Carlson RW, Bonder JJ, et al: Complications of vascular catheterization in the critically ill. *Crit Care Med* 1980; 8:495–499
12. Peters JL, Armstrong R: Air embolism occurring as a complication of central venous catheterization. *Ann Surg* 1978; 187:375–378
13. Green HL, Nemir P: Air embolism as a complication during parenteral alimentation. *Am J Surg* 1971; 121:614–616
14. Feliciano DV, Mattox KL, Graham JM, et al: Major complications of percutaneous subclavian vein catheters. *Am J Surg* 1979; 138:869–873
15. Thomas AN, Stephens BG: Air embolism: A cause of morbidity and death after penetrating chest trauma. *J Trauma* 1974; 14:633–637
16. Ponn RB, Zatarain G, Gerzberg L, et al: Systemic air embolism in experimental penetrating lung injury. *J Thorac Cardiovasc Surg* 1977; 74:766–773
17. Cleveland JC: Fatal air embolism to the right side of the heart during pneumonectomy for carcinoma. *Chest* 1977; 71:556–557
18. Yee ES, Verrier ED, Thomas AN: Management of air embolism in blunt and penetrating thoracic trauma. *J Thorac Cardiovasc Surg* 1983; 85:661–668
19. Tisovec L, Hamilton WK: Newer considerations in air embolism during operation. *JAMA* 1967; 201:376–377
20. Campkin TV, Perks JS: Venous air embolism. *Lancet* 1973; ii:235–237
21. Hybels RL: Venous air embolism in head and neck surgery. *Laryngoscope* 1980; 90:946–954
22. Root B, Levy MN, Pollack S, et al: Gas embolism death after laparoscopy delayed by "trapping" in portal circulation. *Anesth Analg* 1978; 57:232–237
23. Durant TM, Long J, Oppenheimer MJ: Pulmonary (venous) air embolism. *Am Heart J* 1947; 33:269–281
24. Ngai SH, Stirchfield FE, Triner L: Air embolism during total hip arthroplasties. *Anesthesiology* 1974; 40:405–407
25. Spiess BD, Sloan MS, Matz SD, et al: Incidence of venous air embolism in total hip arthroplasty. Abstr. *Anesth Analg* 1986; 65:S170
26. Anderson KH, Halls A: Air aspirated from the venous system during hip replacement. *JAMA* 1984; 251:2720
27. Baggish MS, Daniell JF: Death caused by air embolism associated with neodymium: YAG laser surgery and artificial sapphire tips. *Am J Obstet Gynecol* 1989; 161:877–878

28. Bower FW, Chandra R, Avery GB, et al: Pulmonary interstitial emphysema with gas embolism in hyaline membrane disease. *Am J Dis Child* 1973; 126:117–118
29. Banagle RC: Massive intracranial air embolism: A complication of mechanical ventilation. *Am J Dis Child* 1980; 134:799–800
30. Chiu CJ, Golding MR, Linder JB, et al: Pulmonary venous air embolism: A hemodynamic reappraisal. *Surgery* 1967; 61:816–819
31. Kaufman BS, Kaminsky SJ, Rackow EC, et al: Adult respiratory distress syndrome following orogenital sex during pregnancy. *Crit Care Med* 1987; 15:703–704
32. Bernhardt TL, Goldmann RW, Thombs PA, et al: Hyperbaric oxygen treatment of cerebral air embolism from orogenital sex during pregnancy. *Crit Care Med* 1988; 16:729–730
33. O'Quin RJ, Lakshminarayan S: Venous air embolism. *Arch Intern Med* 1982; 142:2173–2176
34. Doblar DD, Hinkle JC, Fay ML, et al: Air embolism associated with pulmonary artery catheter introducer kit. *Anesthesiology* 1982; 56:307–309
35. Ryan JA, Abel RM, Abbott WM, et al: Catheter complications in total parental nutrition. *N Engl J Med* 1974; 290:757–761
36. Bernard RW, Stahl WM: Subclavian vein catheters: A prospective study. *Ann Surg* 1972; 173:184–190
37. Kloosterboer TB, Springman SR, Cousin DB: Subclavian vein catheter as a source of air emboli in the sitting position. *Anesthesiology* 1986; 64:411–413
38. Mendieta JM, Roy TM, Denny DM, et al: Venous air embolism with removal of central venous catheters. *J Ky Med Assoc* 1988; 86:169–173
39. Ieperen L: Gas embolism as a cause of death. *Am J Forensic Med Pathol* 1985; 6:240–243
40. Kondo K, O'Reilly LP, Chiota J: Air embolism associated with an introducer for pulmonary artery catheters. *Anesth Analg* 1984; 63:871–872
41. Cohen MB, Mark JB, Morris RW, et al: Introducer sheath malfunction producing insidious air embolism. *Anesthesiology* 1987; 67:573–575
42. Conahan TJ, Barberii JK, Calkins JM: Valve competence in pulmonary artery catheter introducers. *Anesthesiology* 1983; 58:189–191
43. Jastremski MS, Chelluri L: Air embolism and cardiac arrest in a patient with a pulmonary artery catheter: A possible association. *Resuscitation* 1986; 14:113–119
44. Adornato DC, Gildenberg PL, Ferrario CM: Pathophysiology of intravenous air embolism in dogs. *Anesthesiology* 1978; 49:120–217
45. Anderson RM, Fritz JM, O'Hare JE: Pulmonary air embolism during cardiac surgery. *J Thorac Cardiovasc Surg* 1965; 49:440–449
46. Berglund E, Josephson S, Ovenfors CO: Pulmonary air embolism: Physiologic aspects. *Prog Respir Res* 1970; 5:259–263
47. Bedford RF, Marshall WK, Butler A, et al: Cardiac catheters for diagnosis and treatment of venous air embolism. *J Neurosurg* 1981; 55:610–614
48. Munson ES, Paul WL, Perry JL, et al: Early detection of venous air embolus using a Swan Ganz catheter. *Anesthesiology* 1975; 42:223–226
49. Presson RG, Kirk KR, Haselby KA, et al: Fate of air emboli in the pulmonary circulation. *J Appl Physiol* 1989; 67:1898–1902
50. Butler SD, Conkin J, Luehr S: Pulmonary hemodynamics, extravascular lung water and residual gas bubbles following low dose venous gas embolism in dogs. *Aviat Space Environ Med* 1989; 60:1178–1182
51. Albertine KH, Wiener-Kronish JP, Koike K, et al: Quantification of damage by air emboli to lung microvessels in anesthetized sheep. *J Appl Physiol* 1984; 54:1360–1368
52. Ohkuda K, Nakahara K, Binder A, et al: Venous air emboli in sheep: Reversible increase in lung vascular permeability. *J Appl Physiol* 1981; 51:887–893
53. Flick MR, Perel A, Staub NC: Leukocytes are required for increased lung permeability after microembolization in sheep. *Circ Res* 1981; 48:344–351
54. Jerome EH, Bonsignore MR, Albertine KH, et al: Timing of corticosteroid treatment. *Am Rev Respir Dis* 1990; 142:872–879
55. Flick MR, Hoeffel JM, Staub NC: Superoxide dismutase with heparin prevents increased lung vascular permeability during air emboli in sheep. *J Appl Physiol* 1983; 55:1284–1291
56. Flick MR, Milligan SA, Hoeffel JM, et al: Catalase prevents increased lung vascular permeability during air emboli in unanesthetized sheep. *J Appl Physiol* 1988; 64:929–935
57. Hlastala MP, Robertson HT, Ross BK: Gas exchange abnormalities produced by venous gas emboli. *Respir Physiol* 1979; 36:1–16
58. Deal CW, Fielder BP, Monk I: Hemodynamic effects of pulmonary air embolism. *J Surg Res* 1971; 11:533–538
59. Butler BD, Luehr S, Katz J: Venous gas embolism: Time course of residual pulmonary intravascular bubbles. *Undersea Biomed Res* 1989; 16:21–29
60. Murphy BP, Harford FJ, Cramer FS: Cerebral air embolism resulting from invasive medical procedures. *Ann Surg* 1985; 101:242–245
61. Gottdiener JS, Papademetriou V, Notargiacoma A, et al: Incidence and cardiac effects of systemic venous air embolism. *Arch Intern Med* 1988; 148:795–800
62. Spencer FC, Rossi NP, Yu SC, et al: Significance of air embolism during cardiopulmonary bypass. *J Thorac Cardiovasc Surg* 1965; 49:615–634
63. Maroon JC, Goodman JM, Horner TG, et al: Detection of minute venous air emboli with ultrasound. *Surg Gynecol Obstet* 1968; 157:1236–1238
64. Coppa GF, Gouge TH, Hofstetter SR: Air embolism: A lethal but preventable complication of subclavian catheterization. *JPEN* 1981; 5:166–168
65. Michenfelder JD, Martin JT, Allenburg BM, et al: Air embolism during neurosurgery. *JAMA* 1969; 208:1353–1358
66. Kashuk JL, Penn I: Air embolism after central venous catheterization. *Surg Gynecol Obstet* 1984; 159:249–252
67. Kuhn M, Fitting JW, Luenberger P: Acute pulmonary edema caused by venous air embolism after removal of subclavian catheter. *Chest* 1987; 92:364–365
68. Clark MC, Flick MR: Permeability pulmonary edema caused by venous air embolism. *Am Rev Respir Dis* 1984; 129:633–635
69. Perschau RA, Munson ES, Chapin JC: Pulmonary interstitial edema after multiple venous air emboli. *Anesthesiology* 1976; 45:364–367
70. Dasher WA, Weiss W, Bogen E: The electrocardiographic pattern in venous air embolism. *Dis Chest* 1955; 27:542–546
71. English JB, Westenskow D, Hodges MR, et al: Comparison of venous air embolism monitoring in supine dogs. *Anesthesiology* 1978; 48:425–429
72. Tateishi H: Prospective study of air embolism. *Br J Anesth* 1972; 44:1306–1310
73. Cucchiara RF, Nugent M, Seward JB, et al: Air embolism in upright neurosurgical patients: Detection and localization by two-dimensional transesophageal echocardiography. *Anesthesiology* 1984; 60:353–355
74. Matjasko MJ, Hellman J, Mackenzie CF: Venous air embolism and end-tidal nitrogen. *Neurosurgery* 1987; 21:378–382
75. Gronert GA, Messick JM, Cucchiara RF, et al: Paradoxical air embolism from a patent foramen ovale. *Anesthesiology* 1979; 50:548–549
76. Alvaran SB, Toung JK, Graff TE, et al: Venous air embolism: Comparative merits of external cardiac massage, intra-cardiac

aspiration and left lateral decubitus position. *Anesth Analg* 1978; 57:166–170
77. Ericsson JA, Gottlieb JD, Sweet RB: Closed-chest cardiac massage in the treatment of venous air embolism. *N Engl J Med* 1964; 270:1353–1354
78. Stallworth JM, Martin JB, Postlethwait RW: Aspiration of the heart in air embolism. *JAMA* 1956; 143:1250–1252
79. Colley PS, Artru AA: Bunegin-Albin catheter improves air retrieval and resuscitation from lethal venous air embolism in dogs. *Anesth Analg* 1987; 66:991–994
80. Bunegin L, Albin MS, Helsel PE, et al: Positioning the right atrial catheter. *Anesthesiology* 1981; 55:343–348
81. Munson ES: Effect of nitrous oxide on the pulmonary circulation during venous air embolism. *Anesth Analg* 1971; 50:785–791
82. Tomatis L, Nemiroff M, Riahi M, et al: Massive arterial air embolism due to rupture of pulsatile assist device. *Ann Thorac Surg* 1981; 32:604–608
83. Cianci P, Posin JP, Shimshak RR, et al: Air embolism complicating thin needle biopsy of the lung. *Chest* 1987; 92:749–751
84. Baskin SE, Wozniak RF: Hyperbaric oxygen in the treatment of hemodialysis associated air embolism. *N Engl J Med* 1975; 293:184–185
85. Bove AA, Clark JM, Simon AJ, et al: Successful therapy of cerebral air embolism with hyperbaric oxygen at 2.8 ATA. *Undersea Biomed Res* 1982; 9:75–80
86. Grim PS, Gottlieb LJ, Boddie A, et al: Hyperbaric oxygen therapy. *JAMA* 1990; 263:2216–2220
87. Catron PW, Dutka AJ, Biondi DM, et al: Cerebral air embolism treated by pressure and hyperbaric oxygen. *Neurology* 1991; 41:314–315
88. Ireland A, Pounder D, Colin-Jones DG, et al: Treatment of air embolism with hyperbaric oxygen. *Br Med J* 1985; 291:106–107
89. Arthur DC, Marguiles RA: A short course in diving medicine. *Ann Emerg Med* 1987; 16:689–701
90. Layon AJ: Hyperbaric oxygen treatment for cerebral air embolism—Where are the data? *Mayo Clin Proc* 1991; 66:641–646
91. Tuman KJ, Spiess BD, McCarthy RJ, et al: Cardiorespiratory effect of venous air embolism in dogs receiving a perfluorocarbon emulsion. *J Neurosurg* 1986; 65:238–244
92. Spiess BD, Braverman B, Woronowicz AW, et al: Protection from cerebral air emboli with perfluorocarbon in rabbits. *Stroke* 1986; 17:1146–1149
93. Menarché P, Pinard E, Desroches AM, et al: Fluorocarbons: A potential treatment of cerebral air embolism in open-heart surgery. *Ann Thorac Surg* 1985; 40:494–497
94. Ellermeyer WP, Keifer P: Central venous cannulation: A new and efficient device. *Anesthesiology* 1986; 65:341–342