

*Primary Care***GAS EMBOLISM**

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GAS embolism, the entry of gas into vascular structures, is a largely iatrogenic clinical problem that can result in serious morbidity and even death.¹ Since gas embolism can result from procedures performed in almost all clinical specialties (Table 1), it is important for all clinicians to be aware of this problem. In most cases, gas embolism is air embolism, although the medical use of other gases, such as carbon dioxide, nitrous oxide, and nitrogen, can also result in the condition. There are two broad categories of gas embolism, venous and arterial, which are distinguished by the mechanism of gas entry and the site where the emboli ultimately lodge.

VENOUS GAS EMBOLISM

Venous gas embolism occurs when gas enters the systemic venous system.² The gas is transported to the lungs through the pulmonary arteries, causing interference with gas exchange, cardiac arrhythmias, pulmonary hypertension, right ventricular strain, and eventually cardiac failure. Physical preconditions for the entry of gas into the venous system are the incising of noncollapsed veins and the presence of subatmospheric pressure in these vessels. Noncollapsing veins include the epiploic veins, the emissary veins, and the dural venous sinuses. Air may enter these veins during neurosurgical operations, especially those performed with the patient in the sitting position.³ The veins of the throat, and in some cases the veins in the coagulated operative field,⁴ may also be entryways for air. Air may also enter veins through central venous and hemodialysis catheters^{5,6} and may enter the veins of the myometrium during pregnancy and after delivery.^{7,8}

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Pathophysiology

The most frequent form of venous gas embolism is the insidious venous aeroembolism, in which a series of gas bubbles resembling a string of pearls enters the venous system. Rapid entry or large volumes of gas put a strain on the right ventricle because of the migration of the emboli to the pulmonary circulation. The pulmonary arterial pressure increases, and the increased resistance to right ventricular outflow causes diminished pulmonary venous return. Because of the diminished pulmonary venous return, there is decreased left ventricular preload, resulting in diminished cardiac output and, ultimately, systemic cardiovascular collapse.⁹ Tachyarrhythmias often develop, but bradycardias are possible as well. When large quantities of gas (over 50 ml) are injected abruptly, acute cor pulmonale, asystole, or both are likely to occur.² The alteration in the resistance of the lung vessels and the mismatch between ventilation and perfusion cause intrapulmonary right-to-left shunting and increased alveolar dead space, leading to arterial hypoxia and hypercapnia.

Diagnosis

To diagnose venous gas embolism, the physician should assess the clinical findings. The so-called mill-wheel murmur, a splashing auscultatory sound due to the presence of gas in the cardiac chambers and great vessels, is often present and can be auscultated by a precordial or esophageal stethoscope. A decrease in the end-tidal carbon dioxide levels, as determined by capnometry, suggests a change in the relation between ventilation and perfusion due to the obstruction of the pulmonary arteries.¹⁰ Doppler ultrasonography is a sensitive and practical means of detecting intracardiac air, and it is often used during neurosurgical procedures,^{3,11} procedures with the patient in the sitting position, and other procedures that entail a high risk of gas embolism. An even more sensitive and definitive method for detecting intracardiac gas is transesophageal echocardiography, although it requires training in performance and interpretation (Fig. 1).^{2,3,12}

Treatment

When venous gas embolism is suspected, further entry of gas must be prevented. In certain cases, therapy with catecholamines is required, and, if necessary, aggressive cardiopulmonary resuscitation is performed. Adequate oxygenation is often possible only with an increase in the oxygen concentration of the inspired gas (up to 100 percent oxygen). Supplemental oxygen also reduces the size of the gas embolus

TABLE 1. MEDICAL SPECIALTIES WITH DOCUMENTED CASES OF GAS EMBOLISM.

SPECIALTY	MECHANISM OF GAS EMBOLISM
All medical specialties	Inadvertent entry of air through peripheral intravenous circuit
All surgical specialties	Intraoperative use of hydrogen peroxide, causing formation of arterial and venous oxygen emboli
Anesthesiology	Entry of air through disconnected intravascular catheter, inadvertent infusion of air through intravascular catheter
Cardiac surgery	Entry of air into extracorporeal-bypass pump circuit, incomplete removal of air from heart after cardioplegic arrest, carbon dioxide-assisted harvesting of peripheral veins
Cardiology	Entry of air through intravascular catheter during angiographic study or procedure
Critical care and pulmonology	Entry of air through disconnected intravascular catheter, pulmonary barotrauma, rupture of intraaortic balloon, entry of air into extracorporeal-membrane-oxygenator circuit
Diving and hyperbaric medicine	Pulmonary barotrauma, paradoxical embolism after decompression injury, entry of gas through disconnected intravascular catheter
Endoscopic and laparoscopic surgery	Entry of gas into veins or arteries during insufflation of body cavities
Gastroenterology	Entry of gas into veins during upper or lower endoscopy or endoscopic retrograde pancreatography
Neonatology and pediatrics	Pulmonary barotrauma in treatment of premature infants
Nephrology	Inadvertent entry of air through hemodialysis catheter and circuit on hemodialysis machine
Neurosurgery	Entry of air through incised veins and calvarial bone, especially during craniotomy with the patient in a sitting position
Obstetrics and gynecology	Cesarean section, gas insufflation into veins during endoscopic surgery, intravaginal and intrauterine gas insufflation during pregnancy
Otolaryngology	Nd:YAG laser surgery on the larynx, trachea, or bronchi*
Orthopedics	Gas insufflation into veins during arthroscopy, total hip arthroplasty, or spine surgery with the patient in a prone position
Radiology	Injection of air or gas as a contrast agent, inadvertent injection of air during angiography
Thoracic surgery	Entry of air into pulmonary vasculature during lung biopsy or video-assisted thoracoscopy, chest trauma (penetrating or blunt), lung transplantation
Urology	Entry of air during transurethral prostatectomy or radical prostatectomy
Vascular surgery	Entry of air during carotid endarterectomy

*Nd:YAG denotes neodymium:yttrium-aluminum-garnet.

by increasing the gradient for the egress of nitrogen from the bubble.¹³ Rapid resuscitation with volume expansion is recommended to elevate venous pressure, thus preventing the continued entry of gas into the venous circulation.

Some authors recommend attempting to evacuate air from the right ventricle with the use of a central venous catheter (a multiorifice catheter may be more effective than one with a single lumen) or a pulmonary arterial catheter.^{2,14,15} It may be possible to aspirate about 50 percent of the entrained air from an appropriately placed right atrial catheter,^{2,14} but depending on the placement of the catheter and the position of the patient, a smaller effect is more likely.^{2,15} Hyperbaric oxygen therapy is not a first-line treatment but may be a useful adjunct in severe cases. It should certainly be considered if there is evidence of neurologic changes. In this case, it should be assumed that a paradoxical embolism is present.

Paradoxical Embolism

A paradoxical embolism occurs when air or gas that has entered the venous circulation manages to enter the systemic arterial circulation and causes symp-

toms of end-artery obstruction. There are a number of mechanisms by which this can occur. One is the passage of gas across a patent foramen ovale into the systemic circulation. A patent foramen ovale, which is detectable in about 30 percent of the general population, makes possible right-to-left shunting of gas bubbles.¹⁶ If there is a patent foramen ovale and if the pressure in the right atrium exceeds the pressure in the left atrium, right-to-left flow through the foramen ovale may occur.¹⁷ Elevated pulmonary arterial pressure due to venous gas embolism may result in elevated right atrial pressure, making it possible for a bubble to be transported through a patent foramen. Furthermore, the decrease in left atrial pressure caused by controlled ventilation and the use of positive end-expiratory pressure may create a pressure gradient across the patent foramen ovale, favoring the passage of gas into the systemic circulation.^{2,3}

In other situations, venous gas may enter the arterial circulation by overwhelming the mechanisms that normally prevent arterial gas embolism. Studies in animals suggest that either a large bolus of gas (20 ml or more) or small continuous amounts (11 ml per minute) introduced into the venous system may

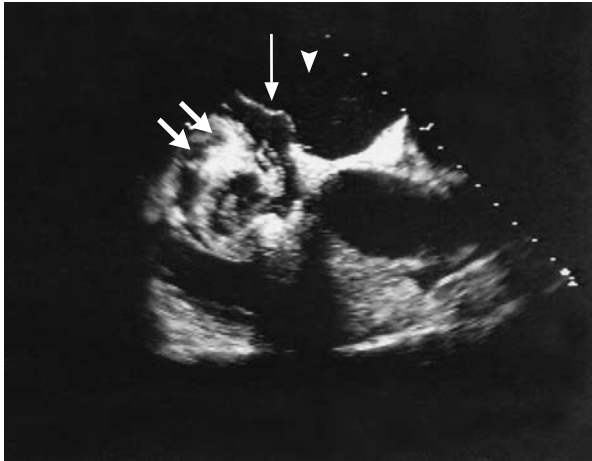


Figure 1. Transesophageal Echocardiogram from a Patient Evaluated for the Presence of a Patent Foramen Ovale.

Saline was agitated and injected rapidly into a central venous catheter. The bubbles appear as echodense areas in the right atrium (double arrows). If this patient had a patent foramen ovale, bubbles would be seen crossing the interatrial septum (thin arrow) and entering the left atrium (arrowhead). (Echocardiogram provided courtesy of S. Streckenbach.)

generate intraarterial bubbles.¹⁸⁻²⁰ There have been reports of fatal cerebral arterial gas embolism caused by a large venous gas embolus, although no intracardiac defects or shunt mechanisms could be demonstrated.²¹ Various anesthetic agents diminish the ability of the pulmonary circulation to filter out gas emboli.²² Studies in animals have shown that volatile anesthetics, specifically, may raise the threshold for a spillover of venous bubbles into systemic arteries. This finding may have relevance to surgical procedures that carry a substantial risk of venous gas embolism.

The treatment of paradoxical embolism is identical to that of primary arterial gas embolism (discussed below). Every venous gas embolism has the potential to evolve into an arterial gas embolism.

ARTERIAL GAS EMBOLISM

Arterial gas embolism is caused by the entry of gas into the pulmonary veins or directly into the arteries of the systemic circulation. Gas may enter the arteries as a result of overexpansion of the lung by decompression barotrauma or as a result of paradoxical embolism. Any cardiac surgical operation that uses extracorporeal bypass may also cause arterial gas embolism.²³ Even if only small amounts of gas enter the arterial system, the flow of gas bubbles into functional end arteries occludes these vessels. Although obstruction is possible in any artery, obstruction of either the coronary arteries or the nutritive arteries of the brain (cerebral arterial gas embolism) is especially serious and may be fatal because of the vulnerability of the heart and brain to short periods of hypoxia.²⁴

Pathophysiology

The entry of gas into the aorta causes the distribution of gas bubbles into nearly all organs. Small emboli in the vessels of the skeletal muscles or viscera are well tolerated, but embolization to the cerebral or coronary circulation may result in severe morbidity or death.

Embolization into the coronary arteries induces electrocardiographic changes typical of ischemia and infarction; dysrhythmias, myocardial suppression, cardiac failure, and cardiac arrest are all possible, depending on the amount of gas embolized.²⁵ Circulatory responses may also be seen with embolization to the cerebral vessels.²⁶

Cerebral arterial gas embolization typically involves the migration of gas to small arteries (average diameter, 30 to 60 μm).²⁵ The emboli cause pathologic changes by two mechanisms: a reduction in perfusion distal to the obstruction and an inflammatory response to the bubble (Fig. 2).²⁴

Symptoms

The symptoms of cerebral arterial gas embolism develop suddenly. The clinical presentation, however, is determined by the absolute quantity of gas and the areas of the brain that are affected. Thus, there may be minor motor weakness and headache or moderate confusion; conversely, complete disorientation, hemiparesis, convulsions, loss of consciousness, and coma may occur.²⁷ Asymmetry of the pupils, hemianopia, and impairment of the respiratory and circulatory centers (manifested as bradypnea, Cheyne–Stokes breathing, cardiac arrhythmias, and circulatory failure)^{25,26} are other well-known complications. In patients who have undergone surgical procedures that carry a risk of gas embolism, a delayed recovery from general anesthesia or a transitional stage of impaired consciousness may be a clue to the occurrence of cerebral arterial gas embolism. The diagnosis is not easy to establish in such patients, because complications of anesthesia, such as the central anticholinergic syndrome or the presence of residual anesthetic or muscle relaxant, can mimic mild cerebral arterial gas embolism.

Diagnosis

The most important diagnostic criterion is the patient's history, because the clinical suspicion of embolism is based on the initial neurologic symptoms and the direct temporal relation between these symptoms and the performance of an invasive procedure. The procedures that carry the greatest risk of venous or arterial gas embolism are craniotomy performed with the patient in the sitting position, cesarean section, hip replacement, and cardiac surgery with cardiopulmonary bypass. All these procedures have in common an incised vascular bed and a hydrostatic gradient favoring the intravascular entry of gas.

Cerebral arterial gas embolism can sometimes be

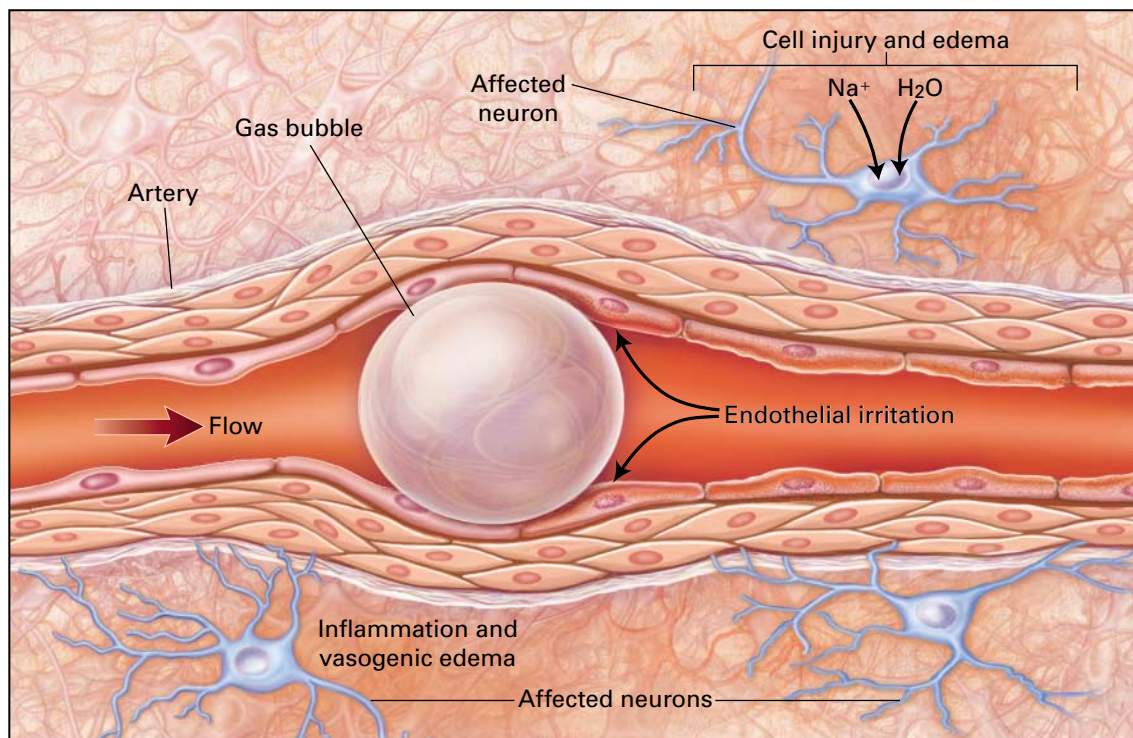


Figure 2. Bubble Obstructing End-Arterial Flow in a Cerebral Vessel with a Diameter of 30 to 60 μm , Causing Distal Ischemia.

The obstruction causes the metabolic processes of neurons to fail. Sodium and water enter the vessel, and cytotoxic edema develops. The surface of the bubble generates a foreign-body response through cellular and humoral immune mechanisms. The bubble also mechanically irritates the arterial endothelium. Both processes result in vasogenic edema and greater impairment of perfusion. The neuronal injury extends beyond the area of obstruction.

distinguished from a cerebral infarct or intracerebral bleeding on a computed tomographic (CT) scan.²⁸ However, pathologic changes are sometimes very subtle and not well visualized on CT, and the diagnosis of cerebral arterial gas embolism must be considered early. Magnetic resonance imaging of the cerebrum can sometimes show an increased volume of water concentrated in the injured tissue. But this method is also not reliable and may fail to detect an embolism if the symptoms are mild.²⁴

Gas bubbles in the vessels of the retina can occasionally be identified, but their absence does not rule out gas embolism.²⁴ Another finding that is nonspecific but that has been described in a number of cases is hemoconcentration with an increase in the hematocrit, possibly as a direct consequence of the extravascular shift of fluid into the injured tissues.²⁹

Treatment

The primary goal of treatment is the protection and maintenance of vital functions. If necessary, cardiopulmonary resuscitation should be performed, since not only venous but also primary arterial gas embolism may lead to serious impairment of the car-

diovascular system. Endotracheal intubation should be performed in a somnolent or comatose patient in order to maintain adequate oxygenation and ventilation. Oxygen should also be administered, at as high a concentration as possible.³⁰ Administration of oxygen is important not only to treat hypoxia and hypoxemia but also to eliminate the gas in the bubbles by establishing a diffusion gradient that favors the egress of gas from the bubbles.^{13,24}

It is currently recommended that patients with arterial gas embolism be placed in the flat supine position.³¹ The buoyancy of gas bubbles is not sufficient to counteract blood flow propelling such bubbles toward the head, even when the patient is placed in a head-down position. In addition, the head-down position may aggravate the cerebral edema that develops in these patients.³²

Treatment of Generalized Seizures

Cerebral gas embolism often causes generalized seizures,²⁷ which may not respond to benzodiazepines. In these cases, it is recommended that the seizures be suppressed with barbiturates.^{27,33} Although there is no proof that barbiturates provide cerebral

protection after cerebral ischemia, the use of barbiturates for ischemic brain lesions has certain advantages. They reduce cerebral oxygen consumption, intracranial pressure, the production of free radicals, and the release of endogenous catecholamines.^{34,35} High doses of barbiturates depress respiration; ventilatory support must therefore be available when a patient is given barbiturates.

Hyperbaric-Oxygen Therapy

With hyperbaric-oxygen therapy, the patient breathes 100 percent oxygen at a pressure above that of the atmosphere at sea level. This therapy decreases the size of the gas bubble both by raising the ambient pressure (Fig. 3) and by causing systemic hyperoxia. An arterial partial pressure of oxygen greater than 2000 mm Hg is frequently achieved. The hyperoxia produces enormous diffusion gradients for oxygen into the bubble and for nitrogen out of the bubble.^{31,32} The hyperoxia also allows much larger quantities of oxygen to be dissolved in the plasma and increases the extent of oxygen diffusion in tissues.²⁷ The improvements in the oxygen-carrying capacity of plasma and in the delivery of oxygen to tissues offset the embolic insult to the microvasculature.

Other benefits of hyperbaric oxygen have been proposed. It may help prevent cerebral edema by reducing the permeability of blood vessels while supporting the integrity of the blood-brain barrier.^{36,37} Furthermore, experiments have suggested that hyperbaric oxygen diminishes the adherence of leukocytes to damaged endothelium.³⁸

These benefits suggest that all patients with clinical symptoms of arterial gas embolism should receive recompression treatment with hyperbaric oxygen. Although immediate recompression produces the best response,²³ delayed treatment in a hyperbaric chamber may still be indicated to ameliorate the patient's condition.³⁹ Hyperbaric oxygen is the first-line treatment of choice for arterial gas embolism.^{23,25,31,40} Thus, as soon as cardiopulmonary stabilization has been achieved, the patient should be transferred to a hyperbaric chamber.

Infusion Therapy

There is some evidence that gas embolism may cause hemoconcentration, which increases blood viscosity and impairs the already compromised microcirculation.²⁹ Therefore, normovolemia should be achieved to optimize the microcirculation. Hypovolemia is always tolerated less well than relative anemia. It is therefore acceptable to decrease the hematocrit, within certain limits. In animals, moderate hemodilution to a hematocrit of 30 percent reduces neurologic damage.⁴¹ Colloid solutions are preferable to crystalloid solutions for hemodilution, because the latter may promote cerebral edema. Hypertonic solutions (e.g., 7.5 percent sodium chloride solution)

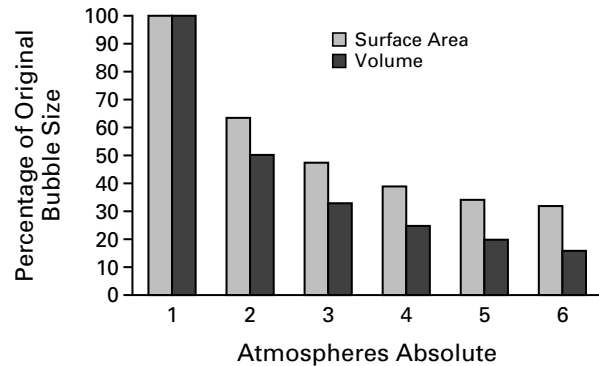


Figure 3. Relation between the Size of the Bubble and Pressure. The surface area and volume of the gas bubble are inversely proportional to pressure at a constant temperature (Boyle's law). Thus, as the patient is exposed to increasing ambient pressure, the gas bubbles shrink.

may become the first choice for volume replacement, but their use is still controversial and therefore cannot yet be recommended.

The goal of infusion therapy is normovolemia. Placement of a central venous catheter is strongly recommended to assess central venous pressure, which should be maintained at approximately 12 mm Hg. As a further method of ensuring adequate volume status, the urinary output should be monitored with a Foley catheter and maintained above 1 to 2 ml per kilogram of body weight per hour.

Anticoagulant Therapy

There is evidence that heparin may be beneficial in the treatment of gas embolism.⁴² Studies have shown that the clinical course of arterial gas embolism is less severe if the patient has been treated with heparin before the embolic event occurs. An argument against heparin therapy is the risk it entails of hemorrhage into the infarcted tissue. At present, the use of heparin for the short-term treatment of cerebral arterial gas embolism is not generally recommended.

Corticosteroid Therapy

The use of corticosteroids in patients with arterial gas embolism remains controversial. Some authors recommend treatment with corticosteroids to combat the brain edema⁴³ that results from gas embolization in the cerebral arteries. Cerebral gas embolism initially induces the rapid development of cytotoxic brain edema, with diminished extracellular space and enlarged intracellular areas. This form of edema does not usually respond to corticosteroids.⁴⁴ Some authors report that corticosteroids aggravate ischemic injury after occlusion of the vessels.^{45,46} Thus, since corticosteroids appear to offer no benefit in patients with cytotoxic edema and since these drugs may aggravate neuronal ischemic injury, we do not recommend them.

TABLE 2. TREATMENT OF GAS EMBOLISM.

TYPE OF TREATMENT	VENOUS GAS EMBOLISM	ARTERIAL GAS EMBOLISM
Prevention of further entry of gas	Measures to increase venous pressure (e.g., Valsalva maneuver or intravenous administration of fluids)	Identification and shutting down of entryway for gas
Primary therapy	Supportive	Hyperbaric oxygen therapy as soon as patient's condition is stable enough for transfer to hyperbaric chamber
Supportive therapy	Oxygen, intravascular volume expansion, catecholamines	Oxygen, intravascular volume expansion, catecholamines
Positioning of patient	Supine, flat	Supine, flat
Evacuation of embolized gas	Aspiration with multiluminal central venous catheter (with patient in left lateral decubitus position)	Hyperbaric oxygen
Adjunctive therapy	Hyperbaric oxygen	Lidocaine, antiepileptic agents, physical therapy

Lidocaine Therapy

Although the results of clinical studies of lidocaine for the treatment of arterial gas embolism are not yet available, studies in animals suggest that lidocaine may be beneficial.⁴⁷⁻⁵¹ In animals given prophylactic doses of lidocaine, the depressant effects of gas embolism on somatosensory evoked potentials and the elevations in intracranial pressure caused by gas embolism were both reduced. In a clinical trial, lidocaine provided cerebral protection during cardiac surgery.⁵¹ Therefore, a strong argument can be made for administering lidocaine in a bolus dose of 1.5 mg per kilogram and maintaining a therapeutic concentration, with continuous intravenous administration in patients with severe arterial gas embolism. However, an overdose of lidocaine may cause central nervous system depression, cerebral convulsions, and bradyarrhythmias.

CONCLUSIONS

The entry of gas into the venous or arterial system is a risk in virtually all areas of clinical care. Venous emboli may lead to cardiovascular collapse or to paradoxical arterial emboli. Arterial emboli may occlude end arteries throughout the body and may cause serious morbidity or death if they occlude cardiac or cerebral vessels.

Regardless of the mechanism responsible for the embolism, rapid and aggressive treatment is essential to preserve life and function (Table 2). For venous gas embolism, the mainstays of treatment are the prevention of further entry of gas, volume expansion, the administration of 100 percent oxygen, often with ventilatory support; positive inotropic support; and cardiopulmonary resuscitation, if necessary. For arterial gas embolism, hyperbaric oxygen is the treatment of choice, as soon as cardiopulmonary stabilization has been achieved.

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