Editorial

Hyperbaric Oxygen Treatment for Cerebral Air Embolism—Where Are the Data?

In this issue of the *Proceedings* (pages 565 to 571), Armon and colleagues present an intriguing case of a cerebral air embolism sustained during the replacement of a mitral valve. Approximately 100 to 200 ml of air passed to the aorta when the atrial vent was inserted. Postoperative seizures and coma resulted, as well as a left-sided paresis. Although funduscopic examination showed no streaming air bubbles, blanched and nonfilled retinal arteries were noted bilaterally; routine therapy (phenytoin and hyperventilation) was begun. Thirty hours after the event, hyperbaric oxygen therapy was initiated. Perhaps because of the hyperbaric treatment, the patient had only mild left hemispheric deficits at 53 days and minimal residua at 14 months after the embolism was sustained. The authors cite this case as evidence that hyperbaric oxygen is the treatment of choice for cerebral air embolism, even if begun late, and their discussion is persuasive.

Several issues need to be addressed:

1. What prospective data show that hyperbaric oxygen is the therapy of choice for cerebral arterial gas embolism?
2. Does the outcome differ between early and late therapy with hyperbaric oxygen?
3. What is the course of cerebral arterial gas embolism with, as opposed to without, hyperbaric oxygen therapy?
4. How is cerebral arterial gas embolism diagnosed? Can neuroimaging studies play a diagnostic role?
5. What is the role of strict management of fluid and glucose in the patient with cerebral arterial gas embolism?

Although it may not be possible to answer each of these questions rigorously, my attempt herein will be to shed light on the infrequently explored areas of hyperbaric oxygen practice.

1. What prospective data show that hyperbaric oxygen is the therapy of choice for cerebral arterial gas embolism? One of the many criticisms leveled at the use of hyperbaric oxygen therapy was that, by 1987, no prospective randomized trials had been conducted to prove its utility in comparison with standard therapy for air emboli.[1] Indeed, a review of the pertinent literature for the past 30 years yielded no prospective, randomized trials in humans or animals that would prove the beneficial effect of hyperbaric oxygen for cerebral arterial gas embolism. One series of reports[2-5] perhaps provides the only data on the subject that approach being definitive. In this series, dogs were anesthetized and were then subjected to instrumentation and to an intracarotid injection of air. Cortical somatosensory evoked potentials, physiologic variables (cardiac output, arterial blood gases, blood pressure, pulse, hematocrit, and cerebrospinal fluid pressure), cerebral perfusion pressure, brain water content, and cerebral blood flow were measured. The animals were treated with either US Navy Table 6 (Fig. 1) or Table 6A (Fig. 2). Although cortical somatosensory evoked potentials deteriorated after air embolization, no significant differences were noted between the treatment groups with regard to rapidity of recovery after compression. Furthermore, no significant differences were found between treatment groups in any factor measured (physiologic variables, cerebral perfusion pressure, brain water content, and cerebral blood flow) even though cortical somatosensory evoked potentials deteriorated significantly after compression in four of five dogs in the Table 6A group.

The literature on humans is perhaps more problematic than the experimental animal work. In a retrospective review of 93 cases of air embolism from various causes, the mortality had been

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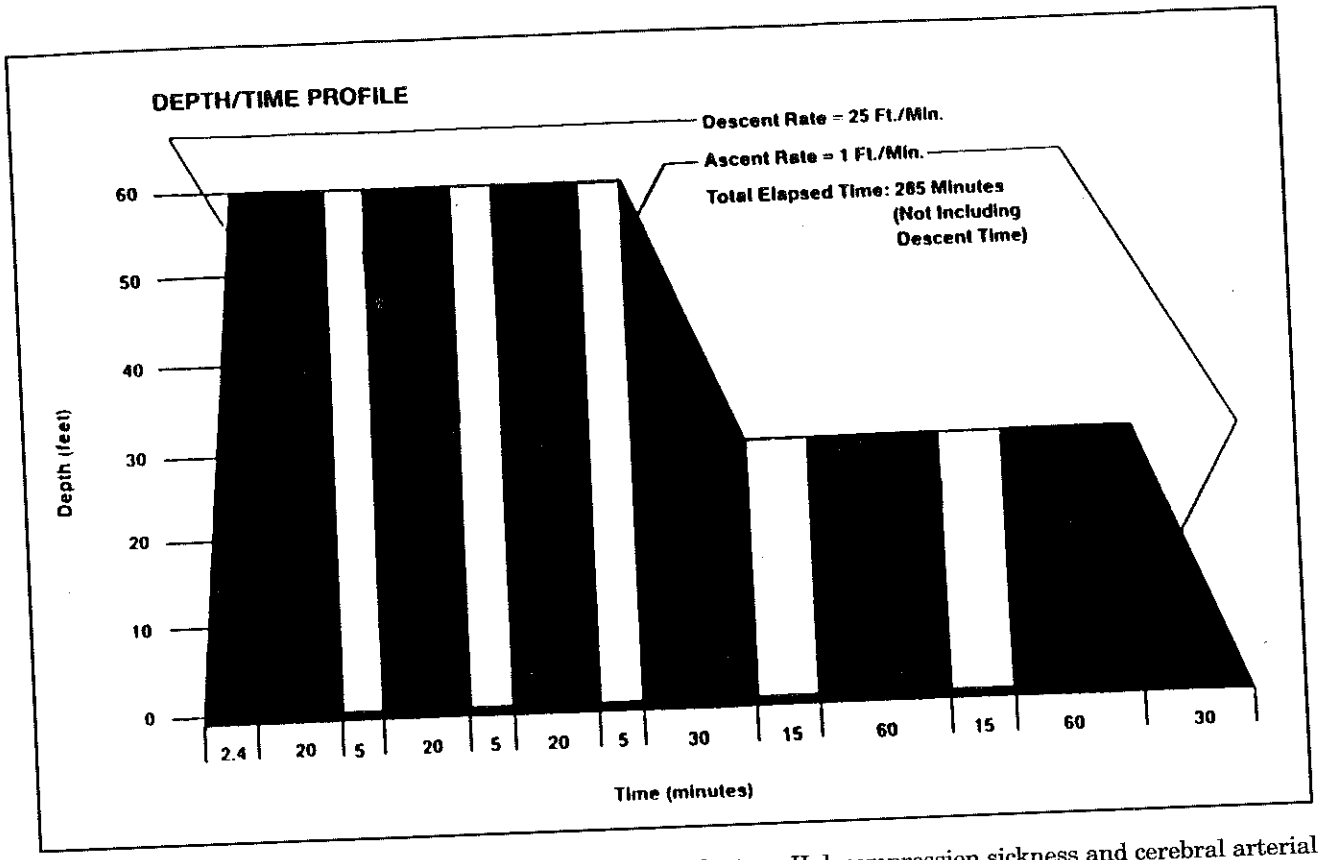

Fig. 1. US Navy Table 6. Air and oxygen treatment table for type II decompression sickness and cerebral arterial gas embolism. Time intervals on horizontal axis refer to time to depth (2.4 minutes), followed by three 20-minute 100% oxygen breathing cycles interrupted by three 5-minute air breaks. This sequence is followed by a 30-minute and then a 60-minute oxygen cycle interrupted by two 15-minute air breaks. Oxygen is breathed continuously during the last 90 minutes. Ascent occurs during a 30-minute period. (From US Navy Diving Manual [NAVSEA 0994-LP-001-9010]. Vol 1: Air Diving. Revision 1. Washington, DC, US Government Printing Office, June 1985, pp 8-36.)

reduced from 93% to 33% by conventional emergency treatment; in that report, conventional therapy was defined as left lateral decubitus positioning, vasopressors, and oxygen under positive pressure.[6] Adding closed-chest cardiac massage to "conventional therapy" decreased mortality to approximately 28%. Because only seven study subjects received cardiac massage, however, the statistical validity is questionable. In another study, each of nine patients who had hemodialysis-associated air embolization was treated with conventional emergency therapy; this therapy resulted in only slight improvement of initial manifestations (predominantly in the cardiopulmonary and nervous systems).[7] Compression to 165 feet seawater (fsw) resulted in dramatic improvement in seven patients within 10 minutes. The other two patients, who required a somewhat more extended treatment regimen, had no signs or symptoms at the conclusion of therapy. A retrospective study of 30 patients with air embolism treated with hyperbaric oxygen (US Navy Table 6) found that all but 6 patients (20%) recovered with minimal to no residua. Four of the six patients had severe residual neurologic findings; two patients died.[8] This outcome represents a 7% mortality rate, in comparison with 33% for those who received conventional emergency therapy.

A decrease in mortality from 93% with no therapeutic intervention, to 28 to 33% with conventional emergency treatment, to 7% with hyperbaric oxygen therapy seemingly provides a strong rationale for the use of hyperbaric oxygen in patients with cerebral air embolism. The comparison of data from different retrospective

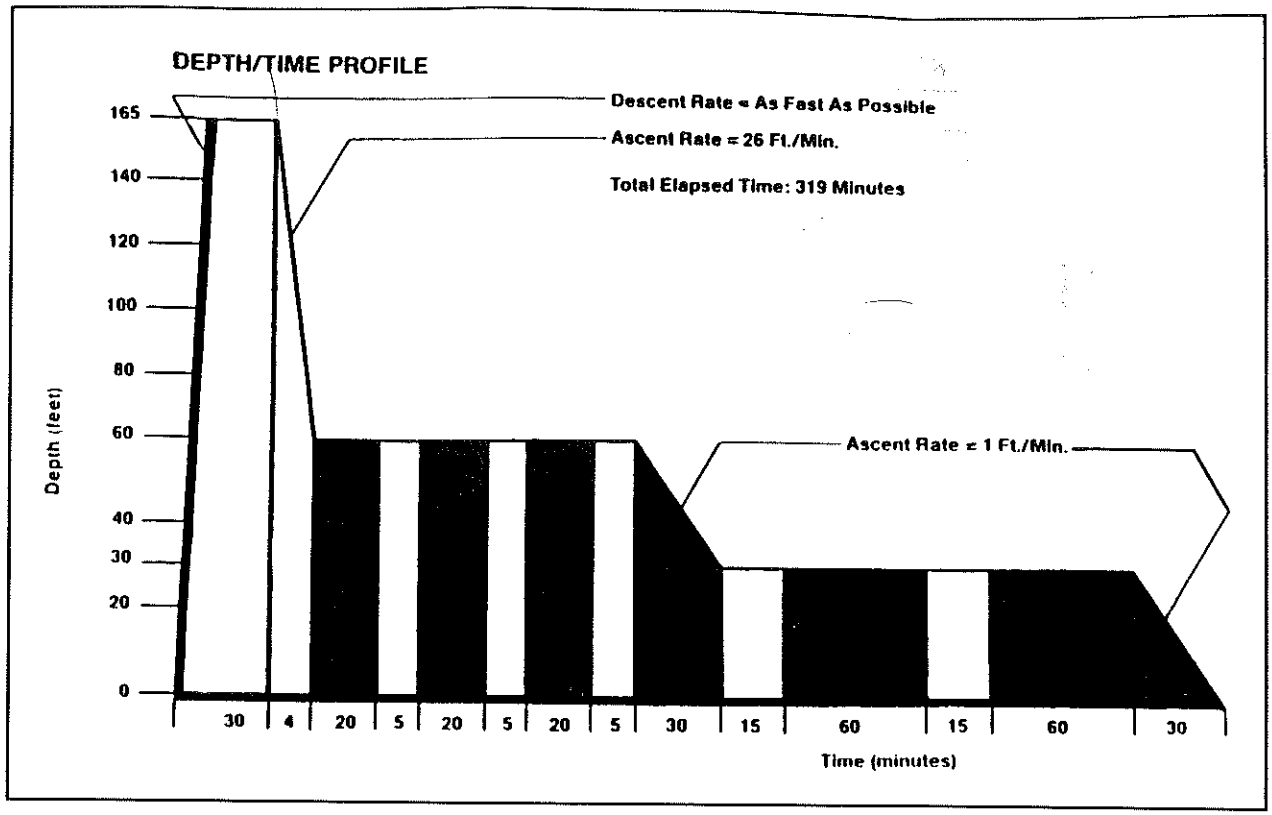

Fig. 2. US Navy Table 6A. Initial air and oxygen treatment table for cerebral arterial gas embolism. The first 30 minutes is spent breathing air at 165 ft. During the next 4 minutes, the depth is decreased to 60 ft; this change is followed by three 20-minute oxygen breathing cycles interrupted by three 5-minute air breaks. The depth is decreased to 30 ft during a 30-minute period while oxygen is breathed. Two 60-minute cycles of oxygen interrupted by a 15-minute air break follow. Ascent to the surface occurs during a 30-minute period while oxygen is breathed. (From US Navy Diving Manual [NAVSEA 0994-LP-001-9010]. Vol 1: Air Diving. Revision 1. Washington, DC, US Government Printing Office, June 1985, pp 8-37.)

studies, however, especially when therapeutic interventions have changed over time, is questionable. Furthermore, I question (although no satisfactory answers are available) whether an iatrogenic air embolus caused by, for example, disconnection of a central venous line is pathophysiologically the same as a cerebral arterial gas embolism that results from rapid ascent from depth with breath holding. At minimum, a prospective, randomized animal study of factors similar to those previously evaluated must be conducted.

2. Does the outcome differ between early and late therapy with hyperbaric oxygen? 30 hours after the occurrence of the embo- ...non and colleagues opted to treat their ... hyperbaric oxygen with US Navy Table 6A followed by US Navy Table 4 (Fig. 3). Would earlier treatment have resulted in a different or better outcome? So late after the initial event, would the patient have recovered even without the assistance of hyperbaric oxygen therapy? These questions have no definitive answers. Many investigators in this area agree that earlier, rather than later, treatment is most appropriate for an air embolus.[3,9,10] The data supporting this statement, however, are anecdotal rather than scientific. No clear distinction exists between "early" and "late" treatment. Davis[10] noted that the classic description of early treatment for cerebral arterial gas embolism is therapy within minutes after the event. This definition apparently originated from the initial cases that were in military and commercial diving

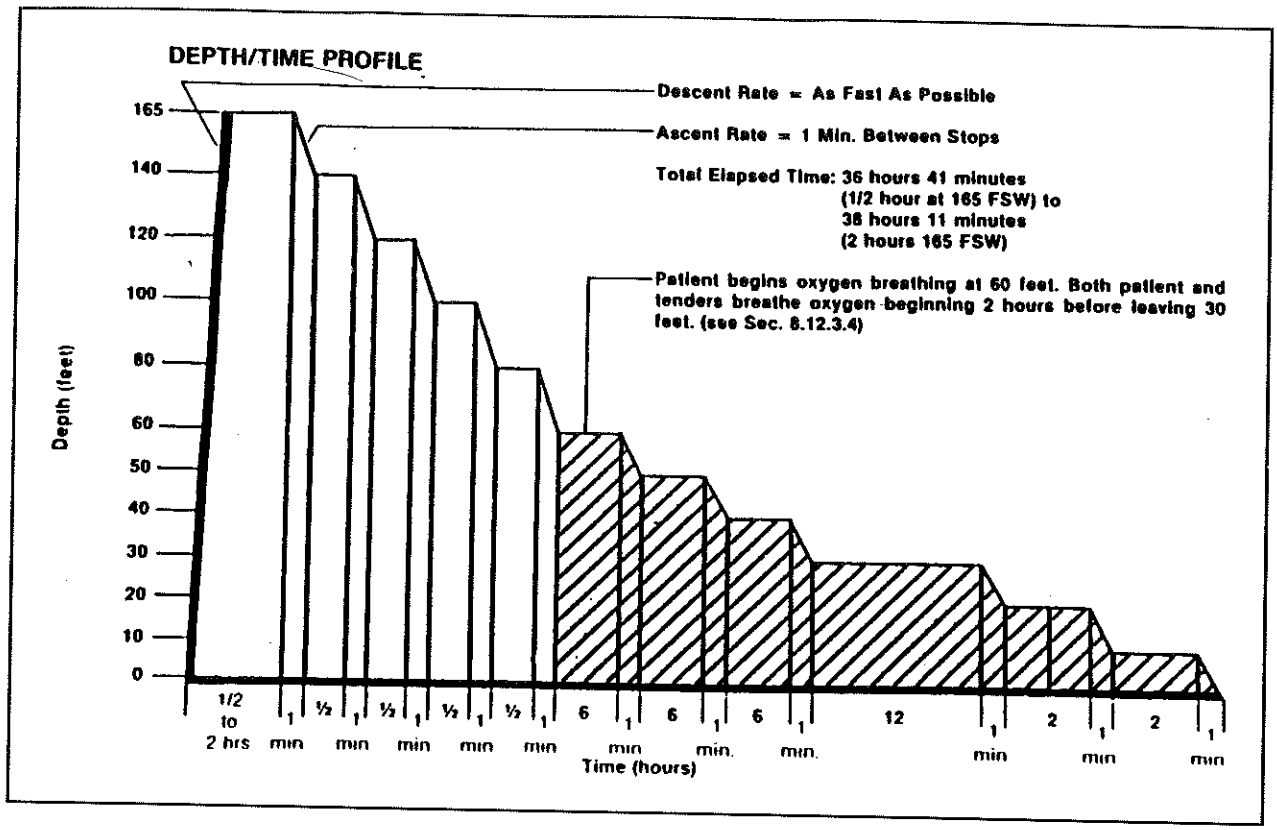

Fig. 3. US Navy Table 4. Air, or air and oxygen, treatment table for refractory type II decompression sickness or cerebral arterial gas embolism. All ascents are made during 1-minute periods. The first ½ to 2 hours (depending on symptoms) is spent breathing air at 165 ft. A ½-hour period at each depth—140 ft, 120 ft, 100 ft, and 80 ft—breathing air follows. At 60 ft, oxygen breathing is begun (20-minute oxygen cycles with 5-minute air breaks) for 6 hours; this period is followed by 6 hours each at 50 ft and 40 ft breathing oxygen or air (or both). The patient is kept at 30 ft for 12 hours; 2 hours before leaving 30 ft, both patient and chamber personnel begin breathing oxygen. Two hours are spent each at 20 ft and 10 ft, during which oxygen is breathed. Ascent from 10 ft occurs during a 1-minute period. The total time encompassed is 38 hours 11 minutes. (From US Navy Diving Manual [NAVSEA 0994-LP-001-9010]. Vol 1: Air Diving. Revision 1. Washington, DC, US Government Printing Office, June 1985, pp 8-38.)

settings where the diagnosis was quickly entertained and treatment facilities were readily available. More recently, sport divers, generally without this type of support, have been stricken. Thus, "late" or "delayed" treatment may mean a hiatus of hours to days after the event. Regardless of the duration of the hiatus, most physicians would consider it appropriate to treat "late" presenters with air emboli aggressively in the hope of obtaining a beneficial response. In my personal (and anecdotal) experience, response—albeit incomplete—is the rule with aggressive therapy, even when initiation is delayed.

Some clinicians advocate different treatment for early as opposed to late presenters with air emboli. Davis[10] asserted that late presenters should be treated only to 60 fsw (US Navy Table 6) rather than the 165 fsw (US Navy Table 6A) to which early presenters are taken. Because Davis provided no rationale for his recommendation, the reasons for this difference are likely based on his extensive experience. At our center, my colleagues and I use Table 6A for both groups. Pertinent available scientific studies,[11] although lacking randomized treatment and having a strong selection bias, suggest that outcome is better with Table 6 than Table 6A or Table 6 with extensions. Until adequate data are available, however, we continue to use Table 6A f our patients with air emboli. Once again, w

designed human or animal studies are needed to clarify these issues.

3. What is the course of cerebral arterial gas embolism with, as opposed to without, hyperbaric oxygen therapy? The approximate mortality rate of 90% in patients with air emboli of various causes can be reduced to 28 to 33% by conventional emergency therapy (left lateral decubitus positioning, vasopressors, administration of oxygen by a mask-valve-bag device, and closed-chest cardiac massage).[6] The use of hyperbaric oxygen therapy has further reduced the mortality to less than 10%[7,8] when either US Navy Table 6 or Table 6A is added. Are these data credible? In my opinion, the answer is an equivocal yes. Nonetheless, one is obliged to ask for well-designed randomized human or animal studies to clarify these issues. It seems generally unwise, except in attempting to define the problem, to compare series of patients treated between 1930 and 1950 with those treated in the 1960s and 1970s.

4. How is cerebral arterial gas embolism diagnosed? Can neuroimaging studies play a diagnostic role? In iatrogenic cases, air embolism is often diagnosed situationally—that is, a change in mental status and a disconnected central venous line are noted, or air in the cardiopulmonary bypass tubing is obvious.[12] For such patients, the differential diagnosis is usually limited and, if a hyperbaric chamber is available, treatment can be instituted rapidly. For divers, the differential diagnosis between neurologic symptoms caused by cerebral arterial gas embolism and those caused by type II decompression sickness usually relates to the rapidity of onset. Furthermore, the former disorder frequently manifests as cognitive dysfunction, whereas the latter often manifests as progressive motor or sensory loss (or both) of the limbs; however, weakness and paresthesias may also occur in some cases of cerebral arterial gas embolism. In virtually all cases, the symptoms of cerebral arterial gas embolism develop within minutes of ascent;[13] type II decompression sickness is usually slower in onset[14] (from minutes to hours) but may manifest almost as rapidly as air embolism. Although in some cases distinguishing between these two conditions will not be possible, treatment with US Navy Table 6 or Table 6A may be used for both.

Several reports[15-18] suggest that, although computed tomographic scanning of the head is of little use, analysis by magnetic resonance imaging, single photon emission computed tomography, or stable xenon-enhanced computed tomographic scanning of regional blood flow may be helpful. The experience at our center with both computed tomographic and magnetic resonance imaging scanning has been less than encouraging.

Thus, no pathognomonic sign or high-technology study allows the definitive diagnosis of cerebral arterial gas embolism. Nevertheless, the rapidity of onset, the type of symptoms, and, perhaps, selected imaging studies will assist in the diagnosis in most cases. Treatment should not be appreciably delayed to obtain these test results.

5. What is the role of strict management of fluid and glucose in the patient with cerebral arterial gas embolism? To date, the role of strict management of fluid and glucose in patients with cerebral air emboli has not been adequately addressed. Because the pathophysiologic features of air emboli include cerebral edema and regional abnormalities in blood flow, in addition to giving corticosteroids, I initiate treatment with one-half to three-quarters maintenance fluid therapy using a solution such as 0.9% saline (osmolarity, approximately 308 mosmol/kg) rather than a more dilute fluid. Furthermore, on the basis of animal work conducted at the Mayo Clinic[19] as well as by others elsewhere,[20] I aggressively control the serum glucose to maintain a concentration of 100 to 150 mg/dl. These variations in treatment are not endorsed by all clinicians; they are within the realm of therapy based on clinical judgment and anecdotal experience. Whether such modifications are of use should be determined by a prospective, randomized trial.

Conclusion.—Armon and colleagues describe a reasonable course of hyperbaric oxygen ther-

apy initiated in a patient 30 hours after she suffered a cerebral air embolism. The patient's recovery after treatment suggests that it was beneficial. The rationale, however, for using hyperbaric oxygen therapy for a substantial number of medical problems is not based on prospective and randomized scientific studies. Such data must be obtained, first in animals (although which model is best suited—cat, dog, monkey, baboon, or piglet—needs some thought and discussion) and then, once focused, in humans.

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