FROM THE HBO_2 INDICATIONS MANUAL14TH EDITION:
CHAPTER 1

Hyperbaric treatment of air or gas embolism: current recommendations

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ABSTRACT

Gas can enter arteries (arterial gas embolism, AGE) due to alveolar-capillary disruption (caused by pulmonary over-pressurization, e.g. breath-hold ascent by divers) or veins (venous gas embolism, VGE) as a result of tissue bubble formation due to decompression (diving, altitude exposure) or during certain surgical procedures where capillary hydrostatic pressure at the incision site is subatmospheric. Both AGE and VGE can be caused by iatrogenic gas injection. AGE usually produces stroke-like manifestations, such as impaired consciousness, confusion, seizures and focal neurological deficits. Small amounts of VGE are often tolerated due to filtration by pulmonary capillaries; however VGE can cause pulmonary edema, cardiac "vapor lock" and AGE due to transpulmonary passage or right-to-left shunt through a patient foramen ovale. Intravascular gas can cause arterial obstruction or endothelial damage and secondary vasospasm and capillary leak. Vascular gas is frequently not visible with radiographic imaging, which should not be used to exclude the diagnosis of AGE. Isolated VGE usually requires no treatment; AGE treatment is similar to decompression sickness (DCS), with first aid oxygen then hyperbaric oxygen. Although cerebral AGE (CAGE) often causes intracranial hypertension, animal studies have failed to demonstrate a benefit of induced hypocapnia. An evidence based review of adjunctive therapies is presented.

Air or gas embolism mechanisms

Gas embolism occurs when gas bubbles enter arteries or veins. AGE was classically described during submarine escape training, in which pulmonary barotrauma occurred during free ascent after breathing compressed gas at depth. Pulmonary barotrauma and gas embolism due to breath holding can occur after an ascent of as little as 1 meter [1]. AGE has been attributed to normal ascent in divers with lung pathology such as bullous disease and asthma [2-3]. Pulmonary barotrauma can also occur as a result of blast injury in or out of water [4-6].

Iatrogenic AGE is due to accidental direct intra-arterial injection of gas. Venous injection of small amounts of gas is not usually problematic because small volumes of VGE bubbles are normally filtered by the pulmonary capillaries and do not cause clinical symptoms. However, in large volumes VGE can cause endothelial injury in pulmonary capillaries and cough, dyspnea and pulmonary edema [7-8]. The capacity of the pulmonary capillary network can also be overwhelmed by large volumes of venous gas, allowing bubbles to enter the arterial circulation [9-10]. VGE can also enter the left heart directly via an atrial septal defect or patent foramen ovale [11-14].

Asymptomatic venous gas embolism (VGE) commonly occurs after compressed gas diving15-16 and after rapid exposure to altitude [17], such as during flight in a military jet, in a hypobaric chamber, or with accidental loss of pressure during flight in commercial aircraft. VGE can occur due to passive entry of air into surgical wounds that are elevated above the level of the heart (such that the pressure in adjacent veins is subatmospheric) [18].

Clinical deficits can occur after intra-arterial injection of only small volumes of air, while intravenous air injection is often asymptomatic. Injection of up to 0.5-1 mL/kg has been tolerated in experimental animals [19]. In humans, continuous IV infusion of oxygen at 10 mL/minute has been reported as well tolerated, while 20 mL/minute has been reported to cause symptoms [20]. Compared with constant infusions, bolus injections are more likely to cause clinical abnormalities [21].

There are several possible mechanisms of injury,

KEYWORDS: arterial gas embolism; air embolism; hyperbaric oxygen

including intracardiac "vapor lock," with resulting hypotension or acute circulatory arrest, and direct arterial occlusion. Animal studies using a cranial window have demonstrated that bubbles can cause a progressive decline in cerebral blood flow [22-23] even without vessel occlusion, an effect that requires neutrophils [24] and can be initiated by bubble-induced stripping of the endothelium from the underlying basement membrane [25-27]. Even without direct mechanical damage, bubble contact with endothelial cells can initiate opening of transient receptor potential vanilloid (TRPV) ion channels, calcium entry, mitochondrial dysfunction and cell death [28-30]. In some cases of cerebral AGE there is clinical improvement followed by delayed deterioration a few hours later [31]. Proposed mechanisms for this include edema, bubble regrowth and secondary thrombotic occlusion.

Manifestations

Manifestations of arterial gas embolism include loss of consciousness, confusion, focal neurological deficits, cardiac arrhythmias or ischemia, while venous gas embolism may include hypotension, tachypnea, hypocapnia, pulmonary edema or cardiac arrest [32-37]. AGE in divers usually presents within a few minutes of surfacing, with cerebral manifestations such as hemiparesis, confusion or loss of consciousness. When the diver has been underwater for a time sufficient to incur a significant inert gas load, gas embolism can precipitate neurological manifestations that are more commonly seen with DCS, such as paraplegia, due to spinal cord damage [38].

Features that support the diagnosis of AGE include rapid or breath-hold ascent or evidence of pulmonary barotrauma (in a diver), evidence of intravascular gas using ultrasound, direct observation (e.g., aspiration of gas from a central venous line) or circumstances consistent with gas embolism occurrence. While imaging studies sometimes reveal intravascular air, brain imaging is often normal even in the presence of severe neurological abnormalities [39-43].

Clinical management and rationale for hyperbaric treatment

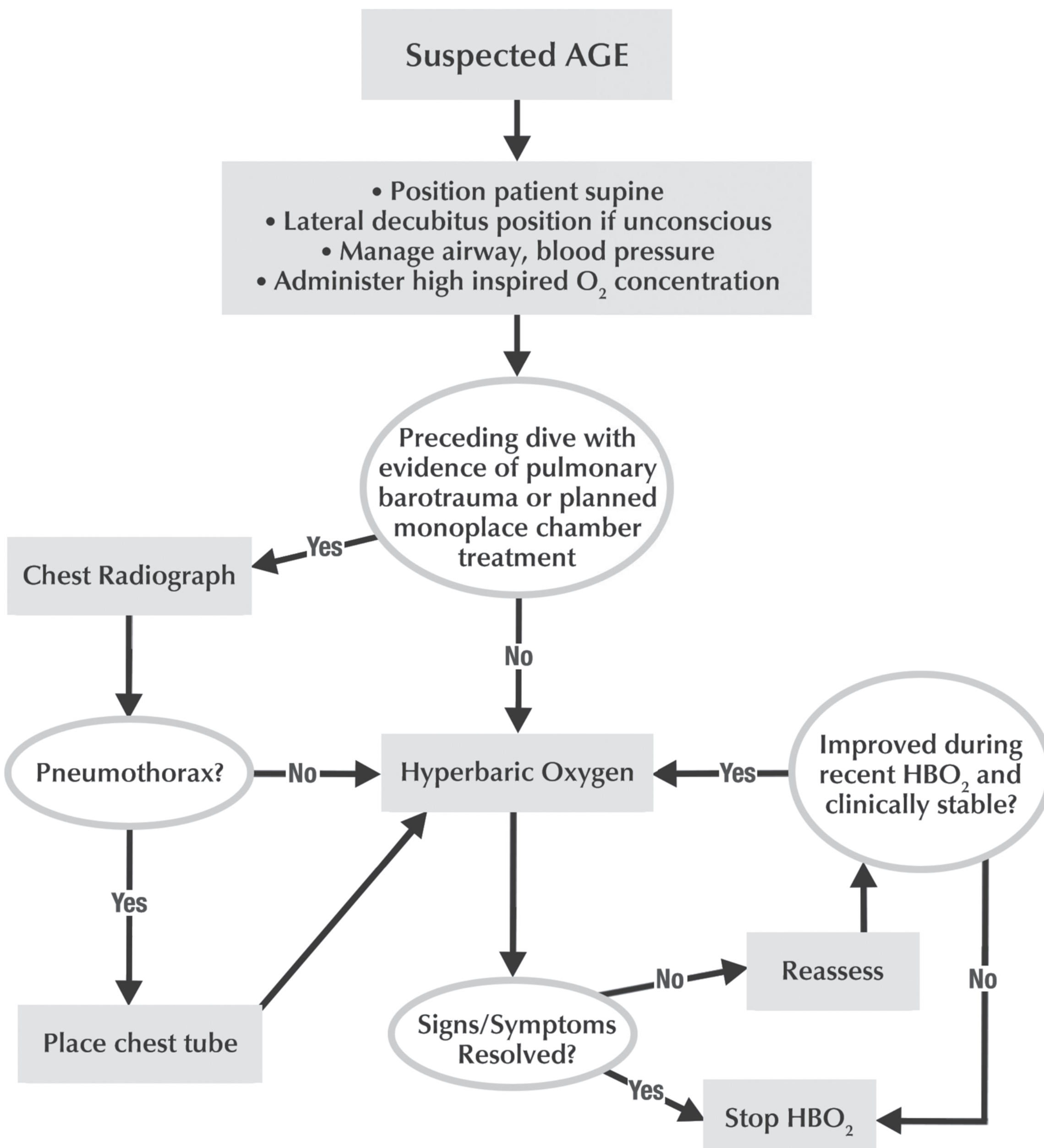
Recognition. The presumptive diagnosis of AGE is made on the basis of clinical criteria. Diagnostic imaging is unnecessary, has low diagnostic sensitivity [4]3 and does not affect management. Absence of intravascular gas should not prevent treatment. Neither CT nor MRI are therefore recommended to attempt to confirm a diagnosis. Performing brain imaging when there is a high degree of suspicion of AGE usually delays the initiation of appropriate HBO_2 treatment and only serves a useful clinical purpose if other pathology is detected that requires different treatment. The only rational reason to perform diagnostic imaging is to exclude other pathology that might have similar manifestations as AGE but require different management (e.g., intracranial hemorrhage).

First Aid. Immediate treatment of gas embolism should consist of airway management, maintenance of blood pressure and administration of as high an oxygen concentration as is feasible. Hypotension can augment the injury and should be actively treated [44]. Supplemental oxygen is recommended not only to maintain arterial oxygenation, but also to facilitate bubble resorption. Nitrous oxide (N_2O) administration causes bubbles to grow, and if gas embolism is suspected in an anesthetized patient N_2O should be discontinued in favor of 100% oxygen.

Head-down position was formerly recommended for the initial treatment of patients with AGE, in order to minimize the risk of additional cerebral embolization because of buoyancy, and shrinkage of bubbles due to increased hydrostatic pressure, and some anecdotal cases support its use [45]. Lateral decubitus position has been recommended in the past for first aid treatment of VGE; however, buoyancy has little if any effect upon arterial [46] or venous [47] distribution of intravascular air. Furthermore, the head-down position can worsen cerebral edema [48]. Head-down position is no longer recommended [49-50]. Recommended first aid for AGE includes placing the patient in the supine position. Unconscious patients should ideally be positioned to maximize airway protection and management: the recovery (lateral decubitus) position [49-50].

Hyperbaric oxygen. HBO_2 to treat gas embolism remains the definitive treatment for arterial gas embolism [51-52] due to the effect of higher ambient pressure to reduce bubble volume, an increase in tissue oxygenation induced by HBO_2 and pharmacological effects of hyperbaric hyperoxia that include inhibition of leukocyte adhesion to damaged endothelium [53-54]. Reviews of published cases of arterial gas embolism reveal superior outcomes with the use of HBO_2 compared to non-recom-pression treatment [32, 36, 55-65]. A short interval between embolism and recompression treatment is associated with a higher probability of good outcome. However, a response to treatment has been observed after 24 or more hours [66]. HBO_2 treatment is not required for asymptomatic VGE; however it has produced clinical improvement in patients with the sole manifestation of secondary pulmonary edema [67].

Figure 1. Flowchart for Management of Arterial Gas Embolism
Details of management are described in the text.



Because of the tendency for patients with AGE to deteriorate after apparent recovery [31], early HBO_2 is recommended even for patients who appear to have spontaneously recovered. One author has suggested that the presence or absence of air detectable by brain computed tomography should be used as a criterion for HBO_2 therapy [68]. However, timely administration of HBO_2 usually causes clinical improvement even in the absence of demonstrable air, possibly due to the effect of HBO_2 to attenuate leukocyte adherence to damaged endothelium [54] and secondary inflammation, and thus facilitate return of blood flow.

In patients with AGE caused by pulmonary barotrauma there may be a coexisting pneumothorax, which could develop into tension pneumothorax during chamber decompression. Therefore, placement of a chest tube in patients with pneumothorax prior to HBO_2 should be considered and is recommended for patients treated in a monoplace chamber. For multiplace chamber treatment, careful monitoring is a feasible option. Coexisting pneumomediastinum does not generally require any specific therapy and will usually resolve during HBO_2.

Immediate recompression to 6 atmospheres absolute (ATA) was recommended in the past. However, there is no conclusive evidence that pressures higher than 2.82 ATA (18 msw, 60 fsw) offer any advantage. If possible, an initial compression to 2.82 ATA (60 fsw or 18 msw equivalent depth) breathing 100% oxygen is recommended, using USN Treatment Table 6 or equivalent. The standards against which other treatment schedules ("tables") should be compared are those of the U.S. Navy (USN Diving Manual [69], available at *http://www.supsalv.org/*) and similar procedures used by other navies and commercial diving operations [70-71]. Shorter tables designed for use in monoplace chambers have been used with success [72]. Significant modification of established HBO_2 treatment regimens have been used in facilities and personnel with the necessary expertise and hardware [70], such that if the clinical response to treatment is judged to be suboptimal, options including deeper recompression or extension of the treatment table can be instituted according to the expertise and resources available.

Administration of repetitive treatments is recommended until there is no further stepwise improvement, typically after no more than one to two hyperbaric treatments, but occasionally up to five to 10 [70-71,73].

More detailed reviews of adjunctive therapies are available in other publications [71,74-76], and a summary can be obtained on the Undersea and Hyperbaric Society website (*www.uhms.org/images/Publications/ ADJUNCTIVE_THERAPY_FOR_DCI.pdf*). Specific adjunctive therapies and their recommendations are listed below.

Adjunctive therapy

Adjunctive therapies for isolated AGE include the following:

- oxygen administered as a first aid measure (class I, level C)
- lidocaine (class IIa, level B)
- aspirin, NSAIDs (class IIb, level C)
- anticoagulants (class IIb, level C)
- corticosteroids (class III, level C)
- intravenous fluids (D5W class III, level C; isotonic crystalloid, colloid class IIb, level C)

Hyperglycemia should be treated, as it worsens acute CNS injury. Although isolated AGE does not require specific fluid therapy, patients with accompanying decompression sickness may have significant hemoconcentration, and require aggressive fluid resuscitation (see Chapter 7: Decompression Sickness in the 14th edition of the HBO_2 indications book). For patients who are immobilized for 24 hours or longer due to neurological injury, low molecular weight heparin is recommended for prophylaxis against venous thromboembolism (class I, level A). In addition, since hyperthermia can adversely affect neurological outcome, aggressive treatment of fever is recommended. There is a plausible rationale for induced hypothermia, which is not yet standard of care but has been reported for AGE due to lung biopsy [77] and in conjunction with HBO_2 for AGE after scuba diving [78]. For critically ill patients with AGE, no systematic human studies are available. In combination with HBO_2, large-animal studies support the use of normotension and isocapnia [44,79-80].

Outcome

While there are no published controlled studies of HBO_2 for AGE, in a retrospective review of 656 published AGE cases, Dutka reported full recovery in 78% of 515 individuals who received HBO_2 vs. 56% of 141 who did not [64]. In the same series the mortality rates were, respectively, 5% and 42%. Of 19 patients reported by Benson with iatrogenic AGE referred for hyperbaric therapy, after the first treatment five patients (26%) resolved all signs and symptoms, 11 (58%) exhibited improvement, one (5%) had no change and two (11%) were not assessable secondary to medically induced paralysis [43]. Within two months post-HBO_2 three additional patients had resolved completely, and six showed further improvement. Eight patients (42%) had complete recovery, six (32%) had partial recovery, and five patients (26%) died of complications of AGE.

In a series of 45 patients treated with HBO_2 for AGE within a single institution reported by Beevor, good neurological outcome (extended Glasgow outcome scale 7 or 8) was achieved in 27 (60%) [81]. The only statistically significant factor predictive of good outcome was time to HBO_2 treatment (good outcome mean 8.8 hours vs.16.5 hours). However, gas bubbles have been known to persist for several days, and there are many reports noting success when HBO_2 treatments were begun after delays of hours to days [61,65,82-83]. In the series reported by Benson, one patient had eventual complete recovery despite a 28-hour time from incident to HBO_2 [43]. In a case

TABLE 1. CAUSES OF ARTERIAL GAS EMBOLISM
DIRECT ARTERIAL AIR ENTRY
Pulmonary barotrauma during ascent from a dive [85]
Mechanical ventilation [86]
Penetrating chest trauma [87]
Chest tube placement [88, 89]
Needle biopsy of the lung [90, 91]
Bronchoscopy [92]
Cardiopulmonary bypass accident [93-95]
Pulmonary bulla rupture during altitude exposure [96-98]
Accidental air injection into a radial artery catheter [99-102]
Vascular air entry due to necrotizing pneumonia [103]
Pulmonary barotrauma from blast injury [157]
Pulmonary overinflation from inhalation of gas under high pressure [158]
VENOUS GAS EMBOLISM WITH SECONDARY ARTERIAL ENTRY VIA PULMONARY CIRCULATION OR INTRACARDIAC RIGHT-TO-LEFT SHUNT
Compressed gas diving [7-10, 15-16]
Rapid exposure to altitude [17]
Accidental intravenous air injection [104-105]
Hemodialysis catheter accident [106]
Central venous catheter placement or disconnection [107-108]
Gastrointestinal endoscopy [109-110]
Esophageal ballooning and endoscopic retrograde cholangiopancreatography [111]
Hydrogen peroxide irrigation [89, 112-118]
Arthroscopy [119-120]
Cardiopulmonary resuscitation [121]
Percutaneous hepatic puncture [122]
Blowing air into the vagina during orogenital sex [61, 123-124]
Sexual intercourse after childbirth [125-126]
Gastric barotrauma following hyperbaric oxygen therapy [127]
Treatment of esophageal cancer128-129]
Atrial-esophageal fistula following ablation for atrial fibrillation [130-133]
PROCEDURES IN WHICH THE SURGICAL SITE IS UNDER PRESSURE
Laparoscopy [134-138]
Transurethral surgery [139-140]
Vitrectomy [141]
Endoscopic vein harvesting [142]
Hysteroscopy [143-144]
PASSIVE ENTRY OF AIR INTO SURGICAL WOUNDS SITUATED ABOVE THE LEVEL OF THE HEART SUCH THAT VENOUS PRESSURE IS SUBATMOSPHERIC [18]
Sitting craniotomy [145]
Cesarean section [146]
Radical perineal prostatectomy [147]
Retropubic prostatectomy [148-149]
Spine surgery [150-151]
Hip replacement [152]
Liver resection [153]
Liver transplantation [154]
Insertion of dental implants [155-156]

report of a 51-year-old diver who lost consciousness within minutes of a 30-meter dive, he remained deeply comatose, intubated and with cardiovascular instability for six days before HBO_2 could be administered. One year after treatment he was leading a functional life [84].

Evidence-based review

The use of HBO_2 for arterial gas embolism and symptomatic venous gas embolism is an AHA class I recommendation (level of evidence C).

Utilization review

Utilization review is recommended after 10 treatments.

Cost impact

The primary treatment of choice for air embolism from any cause is HBO_2 therapy. Decreased high mortality rates and prevention or moderation of permanent neurological damage make this modality cost-effective.

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