Arterial Gas Embolism and Decompression Sickness

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Decompression sickness occurs when a sufficiently large gas phase forms within the tissues of the body after a reduction in ambient pressure. Arterial gas embolism occurs secondary to pulmonary barotrauma when gas is forced into the pulmonary vasculature. Although they may clinically present in a similar fashion, the underlying pathophysiology of the two conditions is quite different.

The physiological problems associated with decompression from elevated atmospheric pressures have been known for over 100 years. These problems can generally be divided into two broad categories: *1*) those due to physical injury as a result of an expansion of gas and *2*) those due to a liberation of a gas phase in tissues. Some of the best clinical descriptions of the latter were published almost a century ago (1, 14).

As an underwater diver descends in the water column, the increasing barometric pressure (0.445 psi/ft of descent) has two major effects. The first is entirely mechanical: any gas-containing space in the body is reduced in volume according to Boyle's law ($P_1V_1 = P_2V_2$). Thus, if one starts off with a volume V in the lungs on the surface and one swims to a depth of 10 m without breathing any additional gas, the volume of gas in the lungs (V) will be reduced to 1/2 V. If one should breathe from a gas source while at that depth (for example, from SCUBA equipment), the lungs will then return to V. Should the diver then swim back to the surface, the volume of gas in the lungs will then expand to 2V. This enlarging volume of gas is usually exhaled, but should there be some reason that the gas is not exhaled (i.e., breath holding), then mechanical forces can result in disruption of lung parenchyma, causing one of the pulmonary overinflation syndromes.

The second major category of physiological problems associated with decompression is based on a different physical principle. As a diver descends in the water column, the partial pressures of the constituent gases he breathes is increased. This then is reflected in alveolar gas, then arterial blood, and eventually increasing amounts of gas are driven into solution in the tissues of the body. Should a diver be using air as the breathing medium, the most important component gas driven into solution is nitrogen. Depending on the amount of gas driven into solution (which is basically a function of depth and time), a varying number or volume of bubbles (gas phase) will form during decompression as a consequence of the reduction in ambient pressure. It is this gas phase that causes the signs and symptoms collectively referred to as "decompression sickness" (DCS).

Pulmonary overinflation syndromes and arterial gas embolism

There are a variety of different pulmonary overinflation syndromes (9). Probably the most common is simple injury to the lung, which manifests itself as local injury hemoptysis, pneumomediastinum, or pneumothorax. Less commonly, overexpanding gas ruptures alveoli and is forced into the pulmonary vasculature. Gas is then distributed systemically, causing arterial gas embolism (AGE) (Fig. 1).

In its classic and most severe form, AGE presents catastrophically (~4% of victims) with collapse, loss of consciousness, apnea, and cardiac arrest. Various theories have been advanced to explain the mechanism of cardiac arrest in these victims. Animal models of carotid artery embolization with gas result in ventricular arrhythmias, and dog models of coronary artery air embolization have also resulted in cardiac arrest. Unfortunately, the course and nature of the ventricular arrhythmias produced by carotid artery embolization does not duplicate the clinical situation in humans, and accidental coronary artery air embolization in humans (in catheter lab misadventures) does not result in sudden cardiac arrest as is seen in victims of AGE. The earliest hypothesized mechanism was "vapor lock" due to filling of the central vascular bed with gas. Unfortunately, injecting gas into a compliant balloon placed into the left ventricle of a dog does not produce cardiac arrest. Thus the exact mechanism by which AGE causes sudden death in humans remains unclear (10).

In victims who do not die suddenly, the signs and symptoms of AGE can be quite varied. Sudden unconsciousness, hemiparesis, marked confusion, and loss of coordination are all consequences of gas embolization to the brain. Frequently, patients will to some degree recover spontaneously from the early and often more dramatic initial signs and symptoms of AGE. Other varied and more subtle signs of the gas embolization may remain, such as abnormalities of the mental status examination. If the initial signs and symptoms are minor and transient, they may be missed entirely.

In the remaining victims of AGE, if the initial signs and symptoms do not resolve spontaneously, neurological deficits of varying severity tend to persist. As noted above, the vast majority of victims will survive the initial insult, and it is only a small percentage who die in the hospital. With treatment, those who survive tend to have a reasonably good prognosis (4).

Although the initial and most obvious signs and symptoms of AGE are due to the distribution of gas emboli to the brain, it

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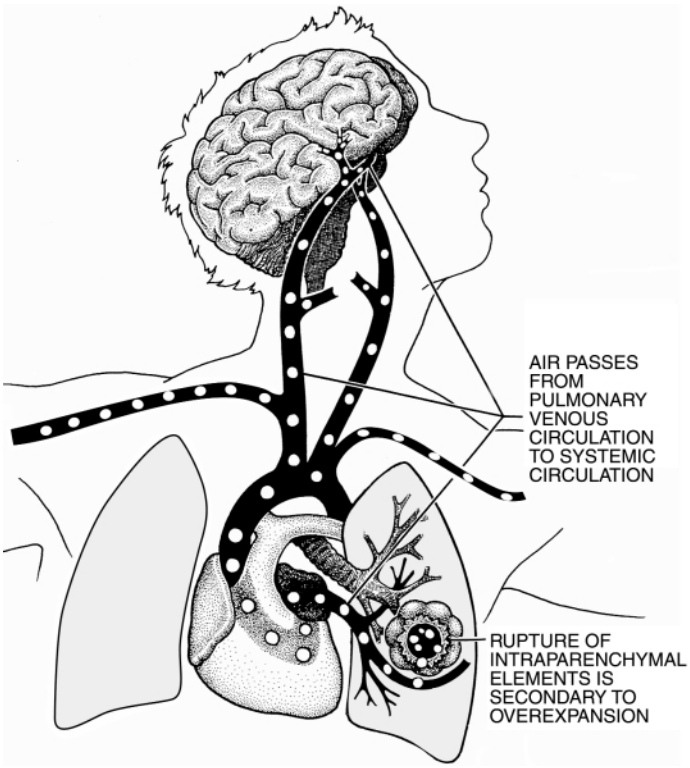

FIGURE 1. Arterial gas embolism.

is now fairly well accepted that gas bubbles are distributed throughout the entire systemic vascular bed. This concept is based on both experimental evidence and clinical observations. Experimentally, gas has been shown to be distributed in the vascular system, not predominately by gravity, but rather by blood flow (2). Clinically, a variety of enzyme and hematologic abnormalities have been described in victims, which suggests that the pathophysiology of the injury due to AGE is much more complex than simple transient obstruction of a portion of the cerebral vascular bed. Indeed, it now appears that the skeletal and hepatic vascular bed as well as the endothelial lining of blood vessels are uniformly affected in the setting of AGE secondary to pulmonary barotrauma (12, 13). What precise role this plays in the pathophysiology of AGE remains to be explored.

DCS

DCS is the term applied to the syndromes associated with the liberation of gas originally held in solution into a free gas phase within the tissues of the body consequent to a reduction in barometric pressure. It is now clear that a gas phase frequently develops in divers before the onset of symptoms that reach the event horizon as overt DCS. This gas phase can most easily be detected in the form of venous bubbles. They are called venous gas emboli (VGE) and can be quantitated and scored by the use of a Doppler ultrasound bubble detector (11). Although there is a general correlation between increasing Doppler scores and the occurrence of clinical DCS, the Doppler bubble grade does not reliably predict which subjects will develop DCS, nor does the peak time of venous bubbles correlate with the onset of symptoms in divers.

In any event, the distribution of gas within the body that is associated with DCS is different from that associated with AGE, and, as a result, the signs and symptoms of DCS are generally different from the signs and symptoms of AGE. Unfortunately, there can be considerable overlap of symptoms, and both AGE and DCS can occur in the same victim. Therefore, there are many clinical situations in which it is impossible to differentiate between the two processes. Nonetheless, there are several "classic" syndromes of DCS that are quite distinct and often easily identifiable (4).

Bends. This is perhaps the earliest, best-described syndrome of DCS. Bends is characterized by deep, boring pain in a large joint. The hips, elbows, and knees are most commonly affected. Symptoms generally occur within 6 h of exposure but on occasion will first develop as long as 12–24 h after exposure. The term probably originated from the similarity between the contorted posture of afflicted caisson workers (due to the pain) and a contemporaneous dance called the "Grecian Bend." Whatever the origin of the term, bends is most often used to describe the syndrome of musculoskeletal pain. Although some authors will use the term only to describe the syndrome of limb pain, most authors will use the term in conjunction with other forms of DCS as well (i.e., spinal cord bends, skin bends, etc.).

Despite the frequent occurrence of limb/joint pain as a manifestation of DCS, surprisingly little is known about its pathophysiology. Clearly, the evolution of gas phase within the joints is not the primary cause. Current theories to explain the symptoms of limb bends are rises in the intermedullary pressure of the ends of long bones and gas phase separation along ligaments and tendon sheaths, causing pain from simple mechanical distention. Supporting a simple mechanical hypothesis is the observation that, as a rule (and if treated early), limb bends is extremely responsive to recompression therapy; oftentimes pain will be relieved as the recompression chamber is still being pressurized and before the victim has reached the "depth" of treatment.

Chokes. When symptoms of cough, substernal chest pain (usually described as burning), and shortness of breath with or without hemodynamic collapse occur, the syndrome is referred to by divers as the chokes. This form of (cardiopulmonary) DCS is thought to be due to an extremely high load of VGE in the pulmonary artery. Although it has not been measured in human victims, it is felt that increased pulmonary artery and right ventricular pressures, possibly associated with the generation of increased interstitial fluid, play a major role in the development of this form of DCS. It is most commonly seen in the period immediately following decompression.

Skin (or skinny) bends. There are a variety of cutaneous signs and symptoms associated with decompression, and not all are specifically classified as DCS. When one is decompressed in a chamber, after a relatively deep and brief exposure in a dry environment, diffuse cutaneous itching is a frequent if not uniform experience. This symptom is thought to be due to transcutaneous passage of gas and therefore is almost never seen

in a wet environment. It is generally considered to be a benign consequence of exposure and not usually treated with recompression. Nonetheless, it is often referred to as "skinny bends." Distinct from this, there is a true form of cutaneous DCS. This is characterized by a diffuse reticulated/blotchy rash called cutis marmorata (marbleized skin) (Fig. 2). This rash is thought to be due to blood extravasated from cutaneous vessels as a consequence of injury to the endothelium from bubbles. Unfortunately, the rapidity with which this rash often disappears (<12 h) makes one question this mechanism. The other form of DCS that is often included with the cutaneous manifestations is lymphatic DCS. Presumably due to mechanical obstruction of lymphatics by bubbles, it manifests itself as lymphedema of the affected area. Most commonly, it is seen over the anterior chest or the flanks. This form of DCS generally presents later than other forms, and the edema, as would be expected, takes days to resolve, even after recompression treatment.

Spinal cord DCS. This is probably the most dangerous form of the commonly encountered syndromes of DCS. It is characterized by ascending parasthesias and paralysis and is frequently associated with bowel and bladder dysfunction. It often affects the lower cervical or lower thoracic regions of the spinal cord, but its predilection for these sites is not understood. Most cases will occur within the first 1–2 h after an exposure. Occasionally, patients will complain of a vague and difficult-to-characterize girdle-like pain preceding the onset of more obvious neurological signs or symptoms.

Currently, there are two major theories to account for symptoms of DCS referable to the spinal cord. Before going into those theories, it is probably worthwhile to dispel the notion that spinal cord DCS is caused by arterial obstruction of the vascular supply to the spinal cord. Most importantly, spinal cord DCS is frequently a bilateral transverse myelitis. For this to be due to arterial obstruction, it would require the routine occurrence of simultaneous obstruction of both the anterior and posterior spinal arteries. In addition, the clinical picture of DCS involving the spinal cord most frequently is that of a progressive ascending myelitis. This often begins as a woolly feeling in the feet that slowly progresses over minutes to an inability to walk, rather than the usual clinical picture of a sudden catastrophic neurological deficit as seen with an anterior or posterior spinal artery syndrome. Looking at animal histopathology in experimental DCS, the distribution of spinal cord abnormalities is not in the pattern of those expected from disruption of the arterial supply to the cord.

The most likely explanation for the signs and symptoms associated with spinal cord DCS are two interrelated mechanisms. The first, and the one for which the best experimental evidence exists, is obstruction of venous outflow of the spinal cord in the epidural plexus. This plexus is a series of blood vessels with a large cross-sectional area and therefore a relatively slow flow. Direct experimental observations in dogs with spinal cord DCS confirm that bubbles will coalesce in this area and eventually lead to complete cessation of blood flow (6). Once this process results in an ongoing and progressive diminution of blood flow to the cord, the second process either begins or is compounded: the in situ formation of a gas phase within the tissue of the spinal cord. Under normal circumstances, following a decompression there is a large gradient for gas to diffuse from tissues into the capillary blood. (Arterial blood is in equilibrium with alveolar gas, and, therefore, the partial pressure of nitrogen in arterial gas is by and large equal to the partial pressure of nitrogen in the atmosphere. Thus there exists a large gradient for nitrogen to leave tissues and enter the blood.) Should the blood flow to tissues decrease, the large amount of gas in the tissues cannot be removed by the volume of perfusing blood, and then the decreasing ambient pressure leads to the formation of bubbles in the tissues (this is referred to as autochthonous bubble formation). Pathological studies in animals suggest that in situ bubble formation takes place, and some of the aspects of the clinical picture of DCS are consistent with the development of in situ bubbles in the spinal cord (5).

The above discussion of AGE and DCS focused mainly on the mechanical effects of bubbles; however, many studies have shown that the pathophysiology of both AGE and DCS are far more complex than the simplistic picture painted above. Bubbles directly injure the endothelium of postcapillary vessels with all of the attendant cellular and humoral responses associated with such injury: platelets aggregate around circulating bubbles, circulatory proteins are affected by the blood bubble interface and orient themselves to alter the relationship of exposed hydrophobic and hydrophilic sites, bubbles accumulate in the pulmonary vascular bed, and neutrophils may be sequestered there. This is only a partial list of the nonmechanical bubble effects, but it should be obvious that these effects can be quite far reaching.

Just as there are tremendous voids in our understanding of these processes at the cellular and biochemical levels, there is also a great deal to be learned about basic relationships between gas absorption and elimination. It is, for example, clear that different exposure profiles generally produce different syndromes of DCS (Table 1). Caisson workers predominantly develop limb bends, as do aviators. Cardiopulmonary DCS is rarely seen in divers, yet before the routine use of oxygen prebreathing death from chokes was an ever-present risk for aviators (7). Recreational divers, especially those doing repetitive dives, will have spinal cord DCS heavily represented

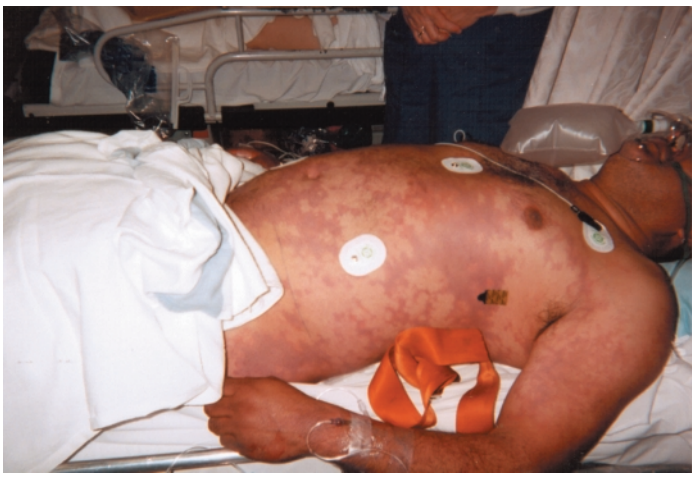

FIGURE 2. Cutis marmorata.

TABLE 1. Initial symptoms of decompression sickness

	Military/ Commercial	Caisson Workers	Recreational Divers
Pain	82	85	41
Sensory changes (parasthesias, numbness)	5.5	1	19
Vertigo/dizziness	3	5	8
Difficulty breathing	0.4	2	2.5

All values are in %. Adapted from Ref. 4.

among their cases; however, aviators and saturation divers essentially never develop spinal cord DCS and caisson workers only rarely develop it. To date, DCS severe enough to require treatment has not been reported in astronauts in space, although VGE are routinely detected (often at quite high bubble grades) in altitude chamber simulations. Another difference between DCS produced by altitude exposure and that seen in divers is the observation that in aviators symptoms of DCS seem to develop at the time VGE are greatest (3). Perhaps a better understanding of the complexities of gas absorption and elimination will one day allow us to better understand the pathophysiology of the different syndromes of DCS.

Another area of considerable importance is the role that "arterialized" gas plays in the pathogenesis of the decompression disorders. Normally a gas phase does not evolve in arterial blood. This is due both to its equilibration with alveolar gas and the higher mechanical pressure within the arteries. On the other hand, bubbles that developed or were transported in the venous circulation can gain access to the arterial circulation by a variety of mechanisms. Bubbles can simply overwhelm the capacity of the pulmonary capillary bed to filter them; they can arterialize through intrapulmonary arteriovenous shunts; and finally they can pass through a patent foramen ovale (PFO) (particularly during a Valsalva maneuver or any other that raises right-sided pressures). Although by no means proven nor agreed upon, there is a developing body of evidence to suggest that PFOs and other right-to-left shunts may play a role in some cases of DCS that otherwise could not be ascribed to the depth/time profile associated with the exposure. As such, arterialized gas bubbles would be expected to be distributed throughout the circulation; the brain would be expected to receive a proportional number of such bubbles. Currently, however, there is no identified chronic brain syndrome associated with diving that would be expected to occur if VGE were routinely passing into the arterial circulation. Because ~25–30% of the population have a PFO and asymptomatic VGE occur in a significant percentage of exposures, ascribing causality to a right-to-left shunt of VGE is probably still premature.

As should be evident from the above description, there can be considerable overlap between both the clinical picture and the underlying pathophysiology of DCS and AGE. Coupled with this clinical overlap, there has been significant confusion over the terms used to describe these entities. One of the early classification systems differentiated DCS into type I or type II. The former consisted basically of limb and skin manifestations, whereas the latter included neurological and cardiopulmonary syndromes (with or without the presence of limb and skin symptoms). The Navy categorized DCS as "pain only" (which also included the cutaneous and lymphatic syndromes) or "serious" (neurological and cardiopulmonary form) primarily because different treatment was prescribed for the different syndromes. Both of the above classifications treated AGE as a separate entity. Because treatment regimens for both AGE and DCS have become similar (and because they are essentially based on symptoms), because of difficulties making a firm diagnosis of AGE or DCS, and because the two frequently coexist (and the former can precipitate the latter under circumstances in which it would not be expected), it has recently been suggested that all of the decompression disorders (including forms of barotrauma not described in this review) be classified on the basis of their symptoms and called decompression illness (DCI). However, this system too has severe limitations. For example, should the object of an experiment be to test a new decompression table, computer, or decompression algorithm for its safety, the inclusion of AGE in the database (which has no relationship to the adequacy of the decompression) would make such an analysis meaningless. Similarly, if the object were to assess whether a given lung disease predisposed divers to idiopathic pulmonary barotrauma (i.e., not caused by breath holding), the inclusion of cases of DCS in the data set (which are presumably related to the depth/time profile of the exposure) would similarly confound the results. Although treatment for AGE and DCS is currently identical, treating both of them as the same clinical entity will not allow researchers to analyze whether advancements in therapeutic regimens selectively benefit one condition more or less than the other. Finally, there still exist forms of decompression injury that are neither DCS nor AGE, which would be classified as DCI, but that require very different treatment. Thus currently there is no completely acceptable classification of decompression-related injuries. From a physiological perspective, it seems most appropriate to maintain a division between AGE and DCS. As a better understanding of the pathophysiology of these injuries evolves, a more mechanistic nomenclature should also evolve.

As mentioned above, the treatment of both DCS and AGE is similar. The mainstay of therapy is recompression. This both mechanically shrinks bubbles and at the same time increases the gradient to drive gas back into solution. Most commonly, patients breathe 100% oxygen during the recompression therapy. This has physiological advantages over air: *1*) it increases the gradient of inert gas (nitrogen) from tissues to the bloodstream; *2*) it hyperoxygenates tissue that is marginally ischemic; and *3*) it may reduce tissue edema by inducing vasoconstriction (secondary to the high arterial P_{O_2}).

In addition to hyperbaric oxygen, there are a variety of other adjunctive treatments that are commonly used. Uniformly, most authorities recommend adequate hydration, because the pathophysiology of both DCS and AGE is felt to include rheologic changes due to extravasation of intravascular fluid as well as the aggregation of formed elements of the blood. Some authorities recommend the use of nonsteroidal anti-inflammatory agents to inhibit platelet aggregation, but others feel the

risk of hemorrhage is too great to use any such agents. Although there has been some animal work in this area, no trials in humans have occurred. Corticosteroids have frequently been used as an adjunct to therapy for both DCS and AGE; however, neither an animal model nor a human clinical trial has shown them to be of any benefit. Finally, lidocaine has been suggested as a possible therapeutic agent on the basis of a beneficial effect in an animal model of AGE and case reports in humans. A clinical trial examining its efficacy in humans with DCS is currently underway (8).

In summary, AGE and DCS remain processes for which the pathophysiology is poorly understood. Ample opportunity remains to study the underlying issues of gas absorption, the effects of a gas blood interface, the mechanical effects of bubbles, the mode by which bubbles form, and the rheologic effects of bubbles.

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