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Letter to the Editor

Gaseous Microemboli and Hyperoxia

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To the Editor:

A recent issue of *JECT* contained two articles on air bubbles in the cardiopulmonary bypass (CPB) circuit and an article on the routine use of hyperoxia during CPB (1–3). Interestingly, these two subjects are related in a way that perfusionists do not commonly associate.

The article by Dickinson et al. (1) and the commentary by Willcox and Mitchell (2) suggested that gaseous emboli passing to the patient from a CPB circuit are, for some patients, inevitable. Some circuits are better than others at removing the potential emboli, but no circuit is 100% safe. The general advice of these authors is to play it safe by preventing air entrainment into the circuit to minimize the potential for gaseous emboli. In other words, nag the surgeon when air bubbles are streaming down the venous line or when the suckers and vent are pumping air-emulsified blood into the cardiotomy reservoir and hope that solves the problem.

How dangerous are these gaseous microemboli (GME)? Recent work by Floyd et al. (4) showed that patients undergoing real "open heart" procedures such as valve replacements and aortic arch reconstructions, wherein air entrainment through the venous line, vent, or suckers is a much greater possibility, have silent (asymptomatic) brain infarcts 18% of the time in addition to the 1.5%–10% of patients who have obvious strokes. The long-term sequelae from these silent infarcts is unknown.

What options does the perfusionist have when confronted with air entrainment? One option is to slow down the pump speed to give bubbles more time to rise in the venous reservoir. But, is this a practical choice? For option 2, volume can be added to the venous reservoir to decrease vortexing. The extra volume also increases the bottom pressure to improve bubble buoyancy. This works for big bubbles, but very small air bubbles have very little positive buoyancy and are much more influenced by fluid current. Once the air bubbles enter the patient's circulation, the only practical option left is "off-gassing." Off-gassing is the treatment for the bends and is the most effective means of removing nitrogen-filled GMEs from a patient's body.

Patients with the bends are usually divers. However, iatrogenic injection of air as GMEs or as gross air embolus as might occur in open heart patients would also qualify as having the bends. Off-gassing usually involves two steps for the patient suffering from the bends. The first, and most important step, is to stop breathing nitrogen-filled air and breathe only 100% oxygen. In the patient who is on CPB, this means using a sweep gas of 100% oxygen. The high concentration of oxygen in the arterial blood does two things. 1) Any nitrogen in the bubbles passing through the oxygenator will quickly off-gas and be replaced by oxygen. If an oxygen bubble passes on into the patient in the form of a GME and obstructs a vital arteriole or capillary, the oxygen will be quickly absorbed and the blockage removed. 2) The high blood PaO_2 and low PaN_2 will quickly off-gas nitrogen from the body tissues. Nitrogen bubbles already trapped in arterioles and capillaries will be removed 10 times faster if 100% oxygen is used compared with room air (5). CPB procedures are usually long enough that nitrogen emboli passed to the patient at the beginning of a case can be entirely removed by the end of the case if the alert perfusionist began using 100% oxygen early.

The second step for treating nitrogen bubbles in the blood requires recompression to at least three atmospheres of pressure. This is not practical with a patient on CPB. However, Figure 1, from the U.S. Navy Decompression Table 5, shows the tolerance humans have for high levels of oxygen. Intermittent breathing of room air for short periods (the "oxygen clock" theory) reduces the stress on antioxidant enzymes that control reactive oxygen species (ROS). It also prevents excessive "on-gassing" of nitrogen during the decompression stages.

This intermittent breathing of room air reduces the potential for oxygen toxicity, which is often confused with ischemic reperfusion injury. Oxygen toxicity occurs when the amount of oxygen present exceeds the antioxidant enzymes' ability to control the production of ROS, whereas the tissue pH remains normal because of the fact that there is no ischemia (6). Oxygen toxicity takes many hours or even days to develop. In ischemic reperfusion injury,

US NAVY TREATMENT TABLE 5 - OXYGEN TREATMENT OF TYPE 1 DECOMPRESSION SICKNESS					
PRESSURE	TIME (min)	MEDIA	pO2 mmHg	pN2 mmHg	TOTAL TIME (hrs:min)
3 ATM	20	100% O2	2280	0	0:20
3 ATM	5	AIR	479	1801	0:25
3 ATM	20	100% O2	2280	0	0:45
3-2 ATM	30	100% O2	2280 - 1520	0	1:15
2 ATM	5	AIR	319	1201	1:20
2 ATM	20	100% O2	1520	0	1:40
2 ATM	5	AIR	319	1201	1:45
2-1 ATM	30	100% O2	1520 - 760	0	2:15
US NAVY DIVING MANUAL, NAVSHIPS 0994-001-9010. WASHINGTON D.C., DEPT. OF THE NAVY, 1991.					

Figure 1. Decompression Table 5 shows how the "oxygen clock" is used to intermittently reduce oxygen stress on antioxidant enzymes during periods of high oxygen exposure under pressure. Without the use of hyperoxia to off-gas nitrogen, decompression treatments for the bends would take 10 times longer.

the antioxidant enzymes are non-functional because of tissue acidosis caused by the ischemia (7–9). Therefore, the ROS caused by even small amounts of oxygen are free to damage vital cellular molecules on reperfusion with oxygen carrying blood. The injury occurs within seconds of the initiation of reperfusion. Once a normal pH is re-established by the reperfusion of tissues with buffered blood, antioxidant enzymes are reactivated and the ROS become controlled.

It is the fear of reperfusion injury that prevents perfusionists from adjusting their sweep gas to 100% to off-gas the nitrogen when they suspect the infusion of GME into the patient. In reality, the amount of oxygen being added to the patient when using 100% FiO_2 is very small. The amount of oxygen available to the tissues that can cause reperfusion injury is much more dependent on the hemoglobin concentration than the sweep FiO_2. Figure 2 looks at two scenarios: one using a low FiO_2 and the other using a high FiO_2. In scenario 1, the patient hemoglobin is 9 g/dL with a PaO_2 of 150 mmHg and a oxygen delivery of 127 ml/L. In scenario 2, the patient hemoglobin is 8 g/dL with a PaO_2 of 500 mmHg and an oxygen delivery of 124 ml/L; which is 3 ml/L less than scenario 1. Either scenario will cause reperfusion injury if the patient is at risk for reperfusion injury because of prior ischemia. Theoretically, the patient in scenario 1 will have greater reperfusion

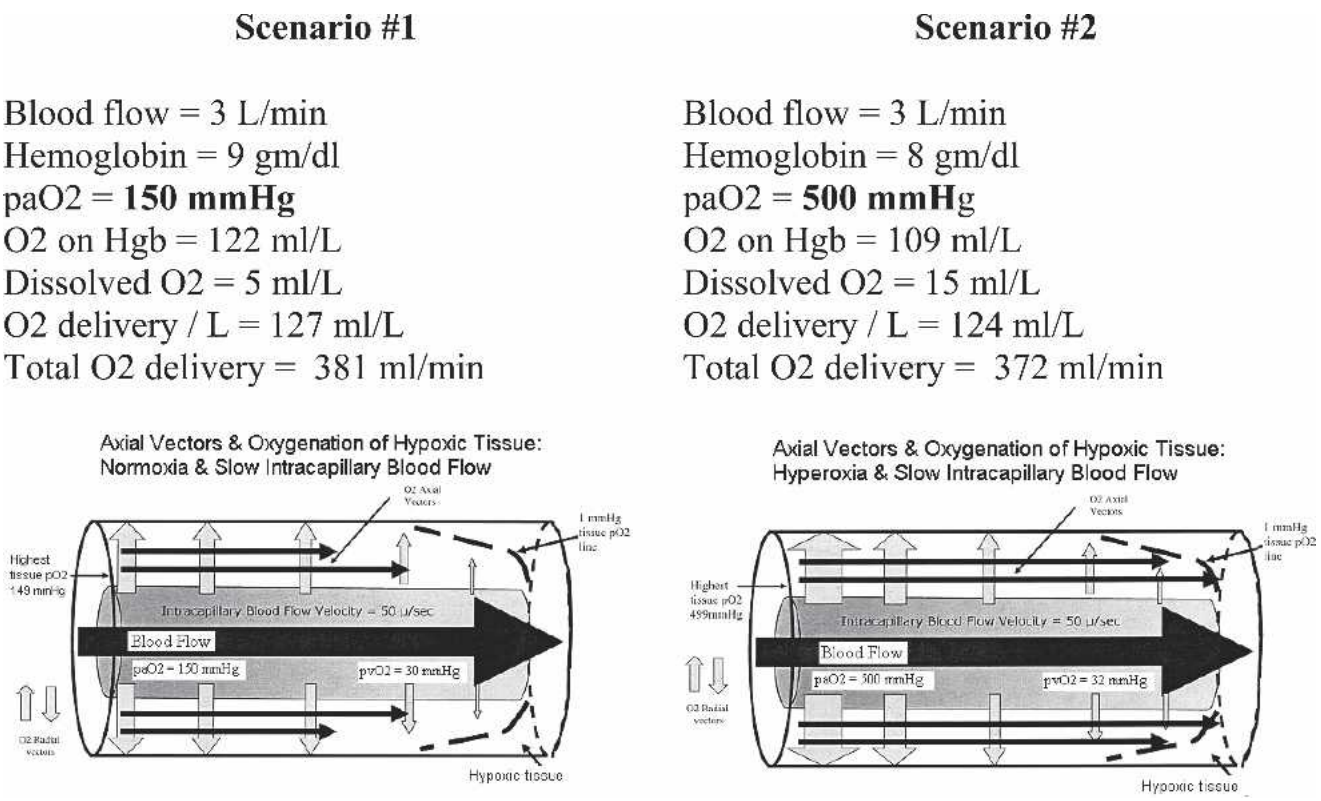

Figure 2. If hyperoxia is defined as an excess of oxygen reaching the tissues, scenario 1 would fit the definition closer than scenario 2. However, because the hemoglobin is abnormally low in both scenarios, neither scenario comes close to creating hyperoxia within the tissues.

injury because more oxygen is being pushed into the tissues than in scenario 2. However, in scenario 2, even though less oxygen is being carried to the tissues, the increased oxygen axial vectors caused by the high PaO_2 will theoretically re-oxygenate oxygen starved tissues more efficiently than in scenario 1 (10).

In reality, patients coming to the operating room for elective surgery are not at risk for immediate reperfusion injury. However, once on CPB, the conduct of perfusion may put the patient at risk for reperfusion injury. If the potential for reperfusion injury develops during CPB, the implementation of hyperoxia at an inappropriate time may aggravate the tissue damage. On the other hand, the implementation of hyperoxia at an opportune time may prevent the potential for reperfusion injury from developing.

The article by Brown et al. (3) shows that the use of hyperoxia on CPB is not fraught with catastrophic complications in the immediate post-CPB period. The greatest danger of reperfusion injury would be when the aortic cross-clamp is removed, and oxygen-filled blood freely flows into the heart. The authors elected to not use the simple tactic of flushing excess oxygen from the oxygenator fiber bundle using room air and turning off the sweep gas just before cross-clamp removal. This would keep oxygen levels low during the short but potentially dangerous period of cardiac reperfusion during which cardiac tissue pH is restored to normal. No such extraordinary precautions were taken in the study because cardiac function apparently returned to adequate levels in both the low PaO_2 and high PaO_2 patients.

While the routine use of hyperoxia during CPB has no distinct advantage over normoxia, the perfusionist should not fear the use of hyperoxia for off-gassing nitrogen during periods when large numbers of GMEs are generated.

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