

LETTERS TO THE EDITOR

Problems Relating to Gaseous Microemboli and the Use of Nitrogen with Bubble Oxygenators

Dear Editor:

The recent editorial by J.B. Riley and colleagues ("Use of Nitrogen in Ventilation of Artificial Blood Oxygenators: A Potential Hazard," *JECT* 16(2):45-46, 1984) warns readers of the danger of substituting nitrogen gas for compressed air when air/oxygen blenders are used with membrane oxygenators. The authors measured the actual percentage of oxygen exiting a blender supplied with nitrogen in place of compressed air, and, not surprisingly, they found lower delivery rates of oxygen than indicated by the dial settings intended for use with compressed room air as the source.

The authors then discussed reports in the literature regarding gaseous microemboli counts, gas removal capabilities of cardiectomy reservoirs, and high arterial oxygen tensions during cardiopulmonary bypass. Their editorial concluded with several specific recommendations among which the authors proposed: "FiN₂ up to .50 is indicated in bubble oxygenator ventilating gas only after decreasing the gas to blood flow ratio fails to decrease the pO₂ and/or adequately remove carbon dioxide. . . ."

Such a recommendation is *not* supported by the literature cited^{1,2} or by consideration of the basic physics of bubbles in blood. In fact, the article by Fries et al. compared the effects of systematic injections of boluses of either oxygen or air bubbles (0.33 to 3.0 ml/kg) into the internal carotid arteries of dogs. These volumes of gases were injected either rapidly (30 to 60 seconds) or slowly (over one hour). Of relevance to cardiopulmonary bypass were the results from the experimental group injected with either air or oxygen slowly. Those animals that had air injected recovered slowly from anesthesia and appeared lethargic after the experiment; nearly all of these animals died. In contrast, those animals that had oxygen injected had the same behavioral changes as the previous group, but "demonstrated a greater

tolerance for equal volumes of oxygen." One of their conclusions was that air emboli were much less well tolerated than oxygen emboli; specifically, twice the volume of oxygen compared with air was required to cause death in 50% of the animals.

Even though the volumes of gas injected in this series of experiments is far greater than the volumes typically infused under the conditions of bubble oxygenator cardiopulmonary bypass, the message of the paper regarding *type* of intravascular gas and its effects is clear. Intravascular air bubbles, 78% of which is nitrogen, are more lethal than oxygen.

In the second article cited in the editorial (Sakauye, et al.) the original study did not substitute nitrogen gas per se for oxygen when ventilating bubble oxygenators, but did use a "modified" room air mixture containing nitrogen. Whereas this may seem academic, the important point is that the total partial pressure of nitrogen in blood is *greater* when substituting 0.50 FiN₂ as recommended by Riley et al. as compared with the substitution of room air (0.50). The study cited demonstrated little or no difference in microemboli counts or volumes of gas captured in a vortex chamber when air was substituted; however, the bubble count is not as important as bubble stability when addressing the problem of intravascular gas bubbles and organ pathology or dysfunction.³

Another major concern with the recommendation in the editorial is based upon the fact that nitrogen, being only one-half as soluble as oxygen,⁴ decreases the rate of resolution of bubbles. Yang et al.⁵ state, ". . . nitrogen gas bubbles have the longest lifetime in the plasma, and consequently also in the blood, than oxygen and carbon dioxide." Since the nitrogen tension in the blood of patients undergoing cardiopulmonary bypass is not well documented, adding additional nitrogen may increase risk if the partial pressure gradients of nitrogen are changed in the direction of the bubbles. Ferris et al.⁶ demonstrated that experimental animals breathing 100% oxygen following air breathing require 27 minutes for venous nitrogen content to decrease by 50% at 20° C., while

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complete whole body denitrogenation under optimal clearance conditions requires 10-12 hours.⁷ With regards to bubble stability, one must also consider the effects of additional gases in solution such as carbon dioxide⁸ and/or residual nitrous oxide⁹.

Other authors have considered the use of other inert gases with bubble oxygenators. Groom et al.¹⁰ have suggested that clinical use of alternative gases with bubble oxygenators should be delayed until further study verifies its safety, while Hlastala and Van Liew¹¹ have warned against of the use of inert gases in patients whose blood is largely saturated with that gas.

While the goal of the editorial was to recommend a technique for achieving more physiologic pO₂ levels, the untested premise that use of nitrogen gas with bubble oxygenators is to be recommended could

prove dangerous to patients and is not supported by any experimental data. Such practice also is contraindicated by the instructions for use supplied by all bubble oxygenator manufacturers. Finally, the fact that nitrogen sources are more readily available than compressed air is not a justification for its use.

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Response

Problems Relating to Gaseous Microemboli and the Use of Nitrogen with Bubble Oxygenators

Dear Editor:

M. Kurusz and Dr. Butler are reacting to recommendation 3b in our recent editorial (*JECT* 16(2): 45-46, 1984); "FiN₂ up to .50 is indicated in bubble oxygenator ventilating gas only after decreasing the

gas to blood flow ratio fails to decrease pO₂ and/or adequately remove carbon dioxide (deduced from² and⁴).” Our references 2 and 4 were Sakauye and associates and C.C. Fries et al. respectively.^{1,2}

Kurusz and Butler's discussion is consistent with our discussion. Additionally, they present a valid argument to suspend oxygen gas bubbles in an oxygenator blood oxygenating column as opposed to nitrogen bubbles.

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Perhaps it would be useful to define our "deduction" of this technique recommendation from Sakauye et al. and Fries et al. works. In the worst case, Sakauye demonstrated an average gaseous microemboli production of $34.1 \mu\text{L}/\text{minute}$ at $4 \text{ L}/\text{min}$ of bovine (hematocrit=35%) blood and $8 \text{ L}/\text{min}$ of 74% nitrogen, 21% oxygen, 5% carbon dioxide gas in a particular bubble oxygenator. During a two-hour perfusion procedure, $4.1 \times 10^2 \mu\text{L}$ of gas will be slowly infused (if an arterial line filter is absent) to the patient. In a 50 kilogram patient this is $82 \mu\text{L}/\text{kg}$, far short of the $.33 \text{ ml}/\text{kg}$ described by Fries et al. that appears to be necessary to cause observable damage in dogs. The use of an arterial line filter with an open bleed line will probably reduce the volume and size of nitrogen microbubbles pumped to a CPB patient. The use of FiN_2 s as great as .50 appears tolerable by CPB patients.

Kurusz and Butler's description of the increased stability of N_2 bubbles in a pO_2 environment less than about 340 mmHg (and pN_2 greater than 340 mmHg) when $\text{FiN}_2 = .50$ is cause to rethink the use of nitrogen in a bubble oxygenator's ventilating gas mixture.

However, the justification or rationalization of

the use of nitrogen gas mixtures in bubble oxygenators is a theoretical, physical, and physiological problem not yet completely defined and studied in human CPB.

The impetus to maintain PaO_2 s less than 200 mmHg during CPB because of increased microembolism may not be valid. The greater microemboli counts may be secondary to greater oxygenator gas flow rates rather than the partial pressure of oxygen alone.

The perfusionist and open heart team are liable for a thoughtful decision to incorporate the use of a room air/ O_2 blender with a bubble oxygenator. The presence of a blender on a heart lung machine does not automatically indicate its use in bubble oxygenators.

We wish to thank M. Kurusz and Dr. Butler for their important communication and valid qualification of this technique recommendation.

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