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The Effects of Preprimed Oxygenators on Gas Transfer Efficiency

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Abstract: Cancellation of on-pump coronary artery bypass grafting after the circuit is primed may result in the discarding of unused circuits. In some off-pump cases, a surgeon may request that the circuit be primed, but complete the surgical procedure without utilizing the circuit. The major concerns about the unused circuit are its sterility and the performance of the oxygenator after it has been primed for a long period of time. The goal of this study is to determine whether prepriming of the circuit with and without albumin has an effect on the gas transfer efficiency of oxygenators during simulated cardiopulmonary bypass. Monolyth integrated membrane lungs (Sorin Biomedical, Arvada, CO) were used to deoxygenate and oxygenate the bovine blood. Oxygenators were preprimed for 72 ($N = 6$) and 24 ($N = 6$) hours before testing. In control group ($N = 6$), oxygenators were tested immediately (0 h) after they were primed. Three different priming solutions were used: physiological saline solution (Group A); 1.25% of human albumin (Group B); and 5% human albumin (Group C). The blood was modified to the American Association of Medical Instrumentation Standards before testing. The blood flow through the oxygenators was set at 2 Lpm and 4 Lpm, with gas (FiO_2 at 1.0) to blood flow ratio at 1:1. Cultures were also obtained from preprimed oxygenators to test circuit sterility. Oxygen transfer in oxygenators primed for 0 h at blood flow of 4 Lpm were 203 mL/min ± 9.7 (Group A), 263.1 mL/min ± 52.9 (Group B), and 270.5 mL/min ± 13.1(Group C, $p < .01$ vs. Group A). In oxygenators preprimed for 72 h, the CO_2 transfers were 135.0 mL/min ± 21.8 (Group A), 104.9 mL/min ± 2.4 (Group B), and 148.9 ± 26.6 (Group C, $p < .006$ vs. Group B). In addition, the pressure drops were 56.5 mmHg ± 5.5 (Group A), 82.6 mmHg ± 13.4 (Group B), and 67.6 mmHg ± 15.3 (Group C, $p < .05$ vs. Group B). In group A, O_2 transfer were 203.5 mL/min ± 9.7 (0 h), 272.4 mL/min ± 66.6 (24 h), and 260.8 mL/min ± 31.1 (72 h, $p < .01$ vs. 0 h). In group B, O_2 transfer were 263.1 mL/min ± 52.0 (0 h), 302.7 mL/min ± 77.4 (24 h), and 235.2 mL/min ± 16.5 (72 hr, $p < .02$ vs. 24 hr). Cultures obtained from 12 preprimed oxygenators presented no organism growth for up to 5 days. In conclusion, oxygen transfer increases in oxygenators preprimed with albumin immediately after they were primed. However, gas transfer decreased after they were primed with albumin for 72 h. Oxygenators preprimed for 24 h and 72 h with 0.9% saline had better O_2 transfer than those primed for 0 h. **Keywords:** albumin, cardiopulmonary bypass, membrane oxygenator, oxygenator performance. *JECT. 2003;35:121–126*

Off-pump coronary artery bypass grafting (CABG) requires that an extracorporeal circuit (ECC) be set up with a perfusionist on stand-by for the duration of the procedure. Typically, the ECC is not primed for an off-pump or minimally invasive procedure unless cardiopulmonary bypass must be emergently initiated. Occasionally, clinical conditions may mandate that the ECC be primed without utilization. If the primed circuit cannot be used within a reasonable amount of time, it is usually discarded. Cancellation of on-pump CABG procedures may also result in the discarding of unused circuits because the ECC is routinely set up and primed in anticipation of scheduled CPB.

Two questions concerning preprimed oxygenator are sterility and performance. Constant care should be taken to prevent contamination of the circuit during assembling and priming the circuit. It has been reported that a circuit primed with Plasmalyte A (Abbott Laboratories, Abbott Park, IL) could be maintained sterile for at least 7 days (1). In many institutions, albumin is used in the priming solution. Whether the presence of albumin in the priming solution promotes bacterial growth remains unknown.

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The performance of hollow fiber membrane oxygenator has been described in several studies (2, 3); however, in tests occurring shortly after priming. The gas transfer efficiency of preprimed oxygenator has not been demonstrated.

The purpose of this study was to determine the effect of prepriming of ECC on gas transfer efficiency of oxygenators during simulated cardiopulmonary bypass.

MATERIALS AND METHODS

Circuit Set Up

The circuit was designed as a single-pass system (Figure 1). The blood path of the circuit was a continuous path from a reservoir, through a roller pump (Stockert Instrumente GMBH, Germany) to the deoxygenator, then to a second reservoir. From the second reservoir, the blood was pumped through the test oxygenator with a roller pump, and back to the first reservoir, which completed the test run. Monolyth integrated membrane lungs (Sorin Biomedical, Arvada, CO) were used to deoxygenate and oxygenate the blood. A CDI (Terumo Cardiovascular System, Ann Arbor, MI) 400 and oxygen saturation monitor (Baxter Healthcare Corp., Irvine, CA) were placed in-line proximal to the deoxygenator and a CDI 100 (Terumo Cardiovascular System, Ann Arbor, MI) were placed in-line distal to this unit. A CDI 500 arterial shunt sensor (Terumo Cardiovascular System, Ann Arbor, MI) was placed within the oxygenator purge line proximal to the blood-sampling manifold. The CDI monitors were calibrated before the start of each experiment and adjusted on an hourly basis according to results of samples drawn from sampling manifolds, and analyzed with the Gem Premier (Instrumentation Laboratory, Lexington, MA) blood gas analyzer (4).

Blood Collection

Fresh bovine blood (less than 6 h) was collected on the morning of each experiment. Approximately 30 liters of the blood were anticoagulated with heparin (5000 iu/L blood) to maintain an activated clotting time of $\geq$480 sec. The blood was modified to the American Association of Medical Instrumentation (AAMI) Standards before testing (see Appendix).

Test Conditions

Groups of six oxygenators were preprimed for 0 (control group), 24, and 72 h before testing (Table 1). Three different priming solutions were used: physiological saline solution (PSS) in Group A; 1.25% of human albumin (ALB-1.25) in Group B; and 5% human albumin (ALB-5) in Group C. The venous blood was circulated through the deoxygenator circuit until AAMI standards were met. This was accomplished by ventilating the deoxygenator with CO_2 balanced with 100% N_2 at 10 L/min with the pump flow at 4 L/min. Once the AAMI standards were verified, the conditioned blood was pumped through the test oxygenator at the blood flow of 2 and 4 Lpm, with a FiO_2 of 1.0 and a gas/blood flow ratio of 1.0. Blood samples were drawn from the inlet and outlet of the test oxygenator and immediately analyzed. The following data were recorded every 30 sec from the inline monitors, pH, $PaCO_2$, PaO_2, SaO_2, SaO_2, Hgb, HCT, base excess/base deficit (BE/BD), and bicarbonate. For the oxygenators preprimed for 72 h, we also performed a stress performance test in which the venous saturation was lowered to

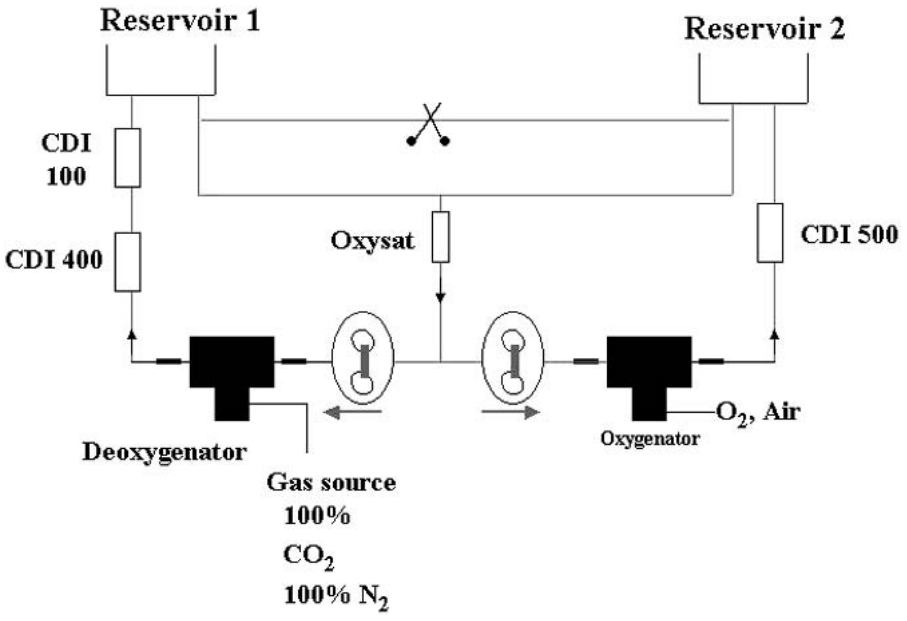

Figure 1. Schematic diagram of the circuit.

Table 1. Experimental groups.

Test Group						Control Group		
Prime for 72 Hours			Prime for 24 Hours			Prime for 0 Hours		
Group A $N = 2$	Group B $N = 2$	Group C $N = 2$	Group A $N = 2$	Group B $N = 2$	Group C $N = 2$	Group A $N = 2$	Group B $N = 2$	Group C $N = 2$
Prime with PPS	Prime with 1.25% albumin	Prime with 5% albumin	Prime with PSS	Prime with 1.25% albumin	Prime with 5% albumin	Prime with PSS	Prime with 1.25% albumin	Prime with 5% albumin

30% at blood flow of 4 LPM. Calculations for oxygen and carbon dioxide transfer are shown in the Appendix.

Sterility Testing

Circuits preprimed for 24 and 72 h were evaluated for sterility (University of Nebraska Medical Center, Division of Clinical Pathology). Five mL of priming solution was collected in sterile fashion from the sample port on the oxygenator. The solution was mixed and processed by aseptically removing 2 mL of the fluid and placing 1 mL each into two thioglycollate broths. Broths were incubated at room temperature and one at 37°C for up to 5 days. If either of the broths became cloudy, a subculture was performed to isolate the organism(s) present.

Statistical Analysis

All data were loaded onto a personal computer in a spreadsheet format. Parametric data were analyzed using a one-way analysis of variance (ANOVA). An additional multiple comparison test (Fisher's least significant difference) was performed when significance was achieved. All data were reported as mean ± standard deviation, unless otherwise stated.

RESULTS

Oxygen Transfer

Oxygen transfer data over the different preprimed time period, priming solution, and blood flow is shown in Table 2. At 0 h, O_2 transfer at a blood flow of 4 LPM was significantly higher ($p < .01$) in ALB-1.25 and ALB-5 primed oxygenators than in PSS primed oxygenator (Figure 2). At 24 h, there was no statistical difference among three priming solutions at both blood flow of 2 and 4 LPM. At 72 h, oxygenator preprimed with ALB-5 had higher O_2 transfer than those preprimed with PSS and ALB 1.25 ($p < .003$, Figure 3). Oxygen transfer in oxygenators primed with PSS was increased significantly over time ($p < .01$, 24 h and 72 h vs. 0 h, Figure 4). However, O_2 transfer on oxygenator primed with ALB-1.25 was decreased at 72 h ($p < .02$, 0 h, and 24 h vs. 72 h, Figure 5).

CO_2 Transfer

CO_2 transfer data over the different preprimed time period, priming solution, and blood flow is shown in Table 3. At 24 h, there was significance difference on CO_2 transfer at blood flow of 2 LPM between PSS, ALB-1.25, and ALB-5 ($p < .05$, PSS vs. ALB-1.25 and ALB-5, Figure 6). CO_2 transfer on oxygenators primed with PSS (Figure 7) and ALB-1.25 (Figure 8) was decreased significantly, comparing with those primed for 24 h and 0 h.

Pressure Drop

The resistance to blood flow was measured as pressure drop across the oxygenator. Oxygenators primed with albumin showed increased pressure drop after they were primed for 72 h. At blood flow of 2 LPM, the pressure drops (mmHg) on oxygenators preprimed for 72 h were 61.6 ± 1.8 (PSS), 79.6 ± 14.5 (ALB-1.25) and 82.0 ± 11.2 (ALB-5, $p < .03$, PSS vs. ALB-1.25 and ALB-5). At blood flow of 4 LPM (Figure 9), the pressure drops were 56.5 ± 5.5 (PSS), 82.6 ± 13.4 (ALB-1.25), and 67.6 ± 15.3 (ALB-5).

Stress Test

When venous oxygen saturation was decreased to 30% in the 72-h group, oxygen transfers were 429.9 ± 28.5 (PSS), 323.7 ± 16.7 (ALB-1.25), and 318.4 ± 42.0 (ALB-5, $p < .05$, PSS vs. ALB-1.24 and ALB-5, Figure 10).

Sterility Testing

Cultures obtained from 12 preprimed oxygenators presented no organism growth for 5 days post-sampling.

Table 2. O_2 transfer.

	0 H		24 H		72 H	
	2 LPM	4 LPM	2 LPM	4 LPM	2 LPM	4 LPM
PSS	112.6 ± 8.5	203.5 ± 9.7	142.2 ± 31.6	272.4 ± 66.6	141.6 ± 15.3	260.8 ± 31.1
ALB-1.25	138.8 ± 20.1	263.1 ± 52.0	161.1 ± 33.1	302.7 ± 77.4	132.0 ± 6.3	235.2 ± 16.5
ALB-5	151.0 ± 14.5	270.5 ± 13.1	140.8 ± 6.2	270.5 ± 13.1	165.3 ± 9.0	282.9 ± 23.8

PSS, physiological saline solution.

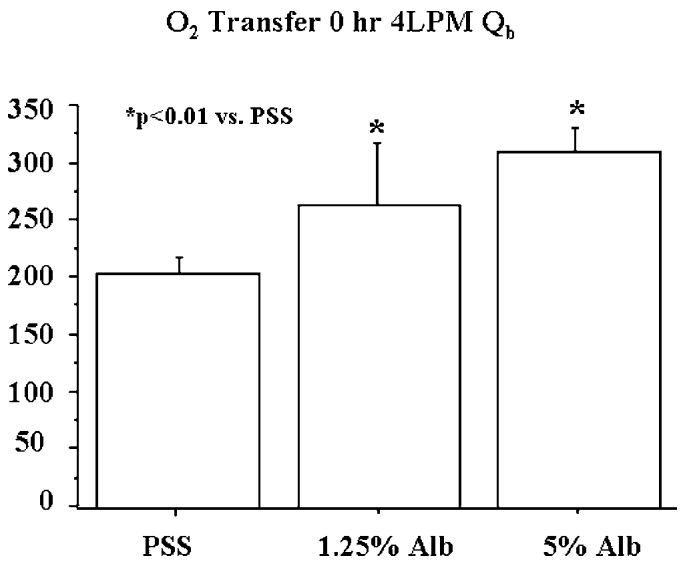

Figure 2. O_2 transfer at 0 h of priming.

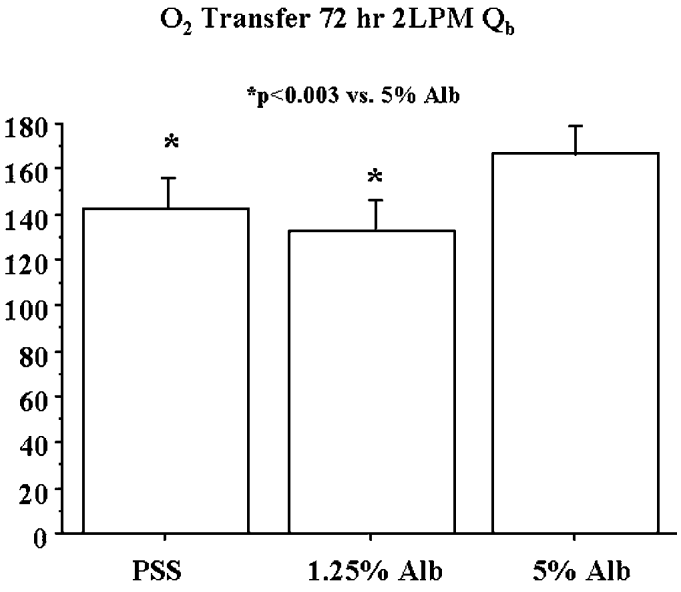

Figure 3. O_2 transfer at 72 h of priming.

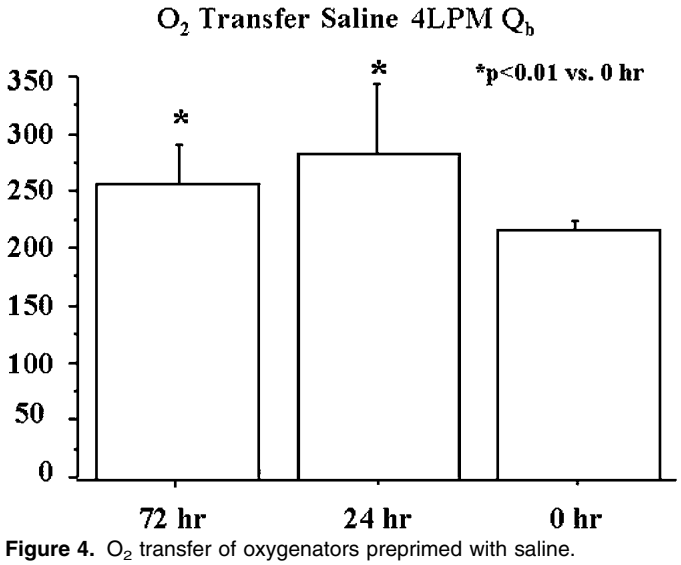

Figure 4. O_2 transfer of oxygenators preprimed with saline.

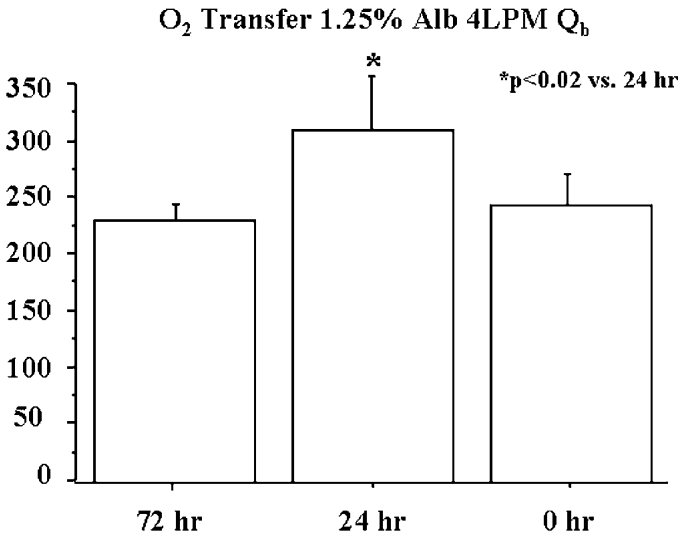

Figure 5. O_2 transfer of oxygenators preprimed with 1.25% albumin.

DISCUSSION

The results of our study are in agreement with others who tested the Sorin Monolyth oxygenator's oxygen transfer rate. Griffith, Vasquez, Beckley, and LaLone (3) showed that the O_2 transfer rate at blood flow of 4 LPM with FiO_2 of 1.0 and blood/gas ratio of 1.0 was 264 ± 13 mL/min. In Gourlay, Aslam, Fleming, and Taylor (2), the O_2 transfer rate at the same condition was estimated at 190 mL/min. Oxygenators in our study resulted O_2 transfer of 203.5 ± 9.7 mL/min.

Albumin is routinely added to priming solutions of the ECC to block protein-binding sites and passivate the ar-

Table 3. CO_2 transfer.

	0 H		24 H		72 H	
	2 LPM	4 LPM	2 LPM	4 LPM	2 LPM	4 LPM
PSS	77.9 ± 3.3	158.7 ± 9.2	84.0 ± 15.6	156.4 ± 24.7	65.2 ± 11.5	135.0 ± 21.8
ALB-1.25	85.2 ± 9.0	158.7 ± 11.6	70.4 ± 14.6	141.4 ± 35.9	49.8 ± 2.1	104.9 ± 2.4
ALB-5	88.1 ± 17.2	161.1 ± 46.9	63.7 ± 5.7	135.0 ± 3.0	59.1 ± 26.1	148.9 ± 26.6

PSS, physiological saline solution.

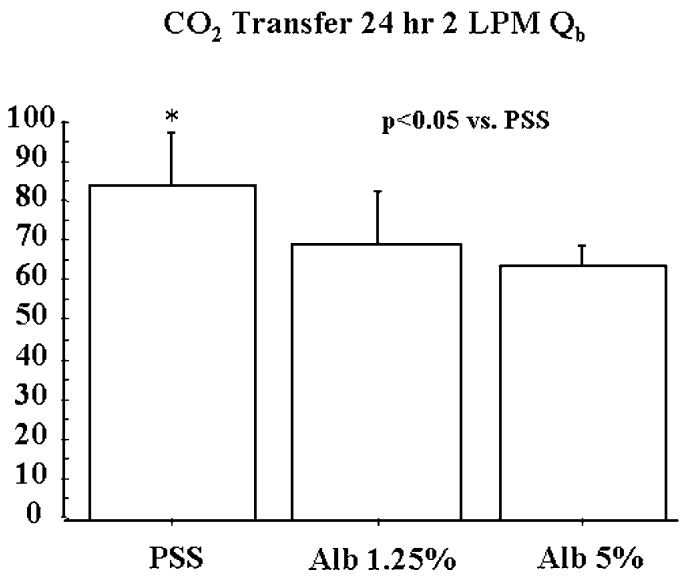

Figure 6. CO_2 transfer at 24 h of priming.

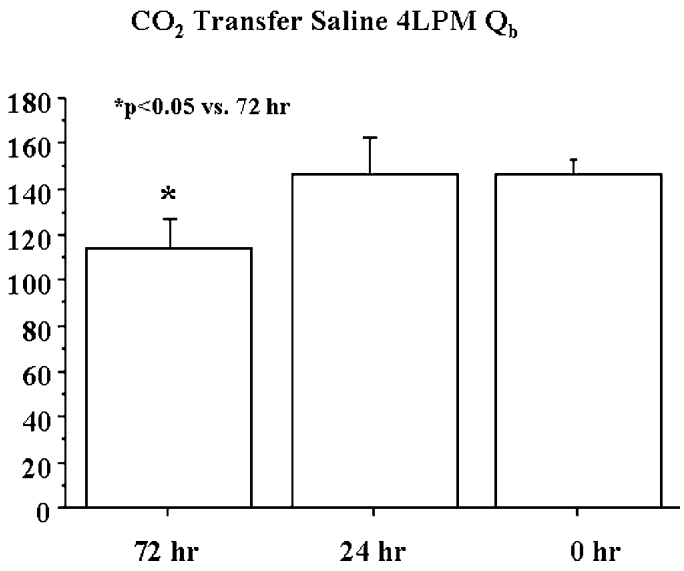

Figure 7. CO_2 transfer of oxygenators preprimed with saline.

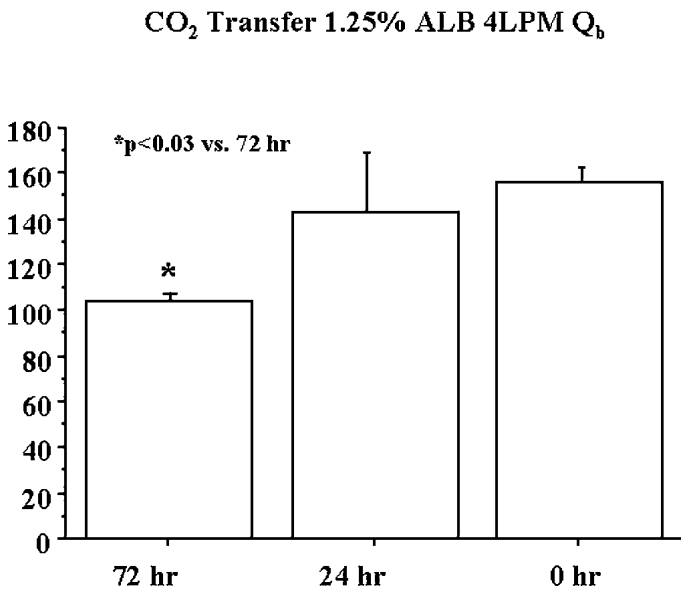

Figure 8. CO_2 transfer of oxygenator preprimed with 1.25% albumin.

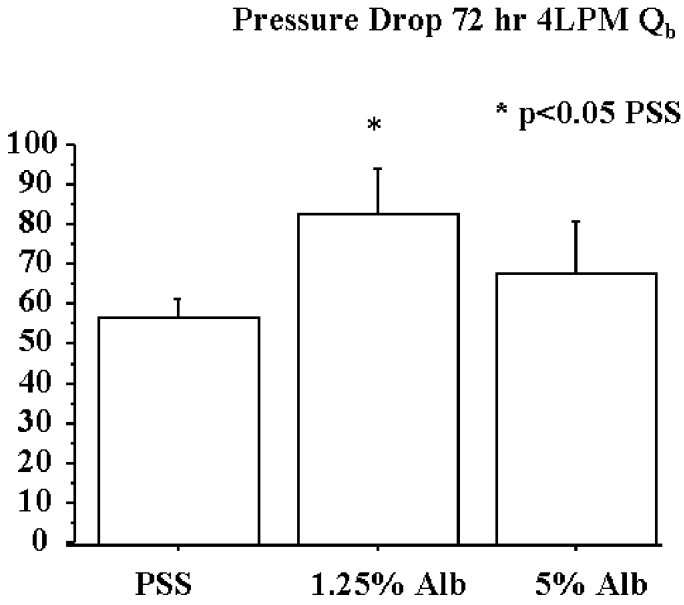

Figure 9. Pressure drop at 72 h of priming.

tificial surfaces before the introduction of blood into the system (5). Our results indicated that O_2 transfer was better in oxygenators that primed with albumin and test at 0 h (Figure 2). However, O_2 transfer rate was decreased at 72 h (Figure 3), but the test was completed without serious decline of function. According to Fick's law of diffusion, O_2 transfer in the membrane oxygenator will vary with the total surface area of membrane, the partial oxygen pressure difference across the membrane, the distance of diffusion, and the permeability of the membrane to oxygen. It is unclear how albumin played a role in O_2 transfer in the oxygenators we tested. It has been hypothesized that albumin acts as a wetting agent, contributing to plasma leakage through microporous membranes. Tamari, Tortolani, and Lee-Sensiba, (6) found that a membrane oxygenator from one manufacturer always failed when albumin was added to the priming solution, but two devices from other companies experienced no failures under test conditions at 78 hours with albumin in the prime. These results suggest that albumin may promote plasma breakthrough for certain types of membrane oxygenators, although the authors note that membrane geometry did not seem to be a factor in plasma breakthrough, but may have been a factor in loss of gas exchange performance. Other in vitro experiments have failed to demonstrate reproducible fluid leakage at high pressures despite the presence of albumin (7).

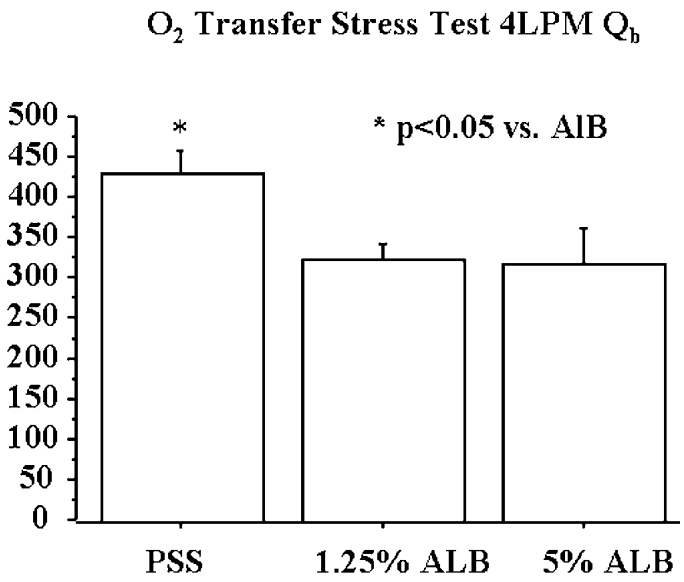

Figure 10. O_2 transfer during stress test.

Our sterility test indicated that even with albumin in the prime solution, no bacterial growth was in the circuit for up to 5 days. This is not an isolated phenomenon and has previously prompted a study of preprimed circuit sterility. Young, Heemsoth, Georgiafandis, Mitchell, Hackett, and Bahna (1) using an open reservoir membrane oxygenator demonstrated that no positive bacterial cultures were obtained over a time period of 168 hours.

Data from laboratory assessment of oxygenator gas exchange may not necessarily accurately reflect gas exchange in a clinical environment. Clayton, Murray, and Pearson note that multiple factors influencing gas exchange during CPB are subject to rapid and unpredictable fluctuation (8). These factors include PaO_2, SvO_2, PCO_2, pH, FiO_2, blood flow, sweep rate, and blood temperature. From their observations, they noted that laboratory figures might overestimate clinical measurements by up to 50% as temperature, FiO_2, and hemoglobin concentrations are much lower during clinical CPB. Griffith, et al. also concluded that laboratory performance data determined under strict, controlled conditions might be of limited value in predicting clinical performance unless modeled to allow for variances in operating conditions (3). Consideration of the effects of variability in hemoglobin concentrations and functionality, blood viscosity, and temperature, and anesthesia or drug interactions should be given when attempting to compare gas exchange data between laboratories and institutions.

In conclusion, preprimed oxygenators presented no bacterial growth in the circuit for up to 5 days. Oxygen transfer increases in oxygenators primed with albumin immediately after they were primed. However, gas transfer decreased after they were primed with albumin for 72 h. Oxygenators preprimed for 24 and 72 h with 0.9% saline had better O_2 transfer than those primed for 0 h. Our findings further promote the use of albumin in the priming solution of an oxygenator, although the performance of such primed oxygenators decreased over time.

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APPENDIX

O_2 TRANSFER RATE: Fick Principle–
$TO_2 = [(\text{Art. Sat} - \text{Ven. Sat}) \times 1.34 \times \text{Hgb} + \text{Sol}\ (pO_2)] \times \text{flow (dL/min)}$
CO2 TRANSFER RATE:
$TCO2 = (PaCO_2 \times Va)/0.863$
Va = Ventilation Rate
AAMI Standards for Blood Inlet Conditions:
Oxyhemoglobin Saturation 65 ± 5%
Hemoglobin Content 12 ± 1 gm%
Base Excess 0 ± 5 mEq/L
PCO2 45 ± 5 mmHg
Temperature 37 ± 1°C