A Simplified *In Vitro* System for Evaluating Gas Transfer Characteristics of Oxygenators

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Introduction

Despite the excellent performance of membrane oxygenators, bubble oxygenators continue to dominate routine open heart surgery. Newer versions with reduced gas:blood flow ratios continue to appear for clinical application[1,2]. The new models generally provide data on partial pressure of oxygen (pO_2) of oxygenated blood at given blood and oxygen flow rates from clinical perfusions[3-7]. Clinical data has admitted drawbacks in evaluating the candidate oxygenator. Thus there would seem to be a need for a simple *in vitro* system for evaluating the performance of an oxygenator. Such a system should offer close control over such parameters as hemoglobin content, temperature pH, pCo_2, pO_2 and percentage oxygen saturation. Control of such functional parameters is difficult, if not impossible in *ex vivo* experiments, thanks to the variable hemodynamic responses of the experimental animals. This paper describes a simple *in vitro* test setup which offers easier and more accurate control of blood gas parameters than the conventional *ex vivo* and *in vitro* systems.

Figure 1 illustrates a conventional circuit used for the evaluation of an oxygenator[8-10,14]. The blood circuit incorporates a deoxygenator system consisting of two bubble oxygenators and venous and arterial reservoirs. A calibrated pump gives controlled blood flow into the test oxygenator. About 4–6 liters of blood are used to prime the circuit. The blood temperature is maintained at the desired level with a heat exchanger. Controlled flow of nitrogen and carbon dioxide deoxygenates the blood. Since it is often necessary to recirculate the blood through the deoxygenator to bring down the percentage oxygen saturation to the required level (60–65%), a recirculating pump is incorporated in the circuit. In essence, the conventional systems are closed loop systems utilizing the principle of continuous deoxygenation and oxygenation of blood. Our experience with the closed loop system has been unsatisfactory in so far as deoxygenation was insufficient at higher blood flows of 3–5 LPM. The resulting rise in the oxygen saturation of venous blood demanded corrective efforts which made the circuit more elaborate, complex and frequently unstable. This has also been the experience of earlier workers[10]. We therefore elected to use a simpler system, which has enabled us to achieve easier and closer control of input blood parameters.

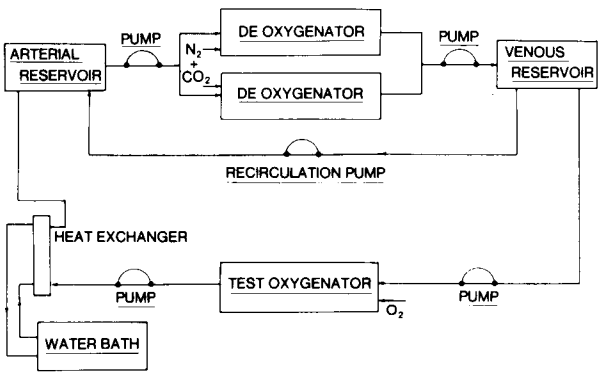

FIGURE. 1. Schematic Diagram of a Conventional Oxygenator—Deoxygenator System.

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TABLE I
Venous Blood Parameters For Oxygenator Testing (Literature Summary)

Parameter	Galletti[11] et al.	Ward[12] et al.	Std. Committee[13] ASAI0	Nose[14] et al.
Hemoglobin g%	—	14 ± 0.7	12 ± 1.0	—
Hematocrit %	40	40	—	40 ± 2
Temperature °C	37–38	39 ± 1	37 ± 0.5	37 ± 0.5
pH	—	7.35 ± 0.1	BE = 0	7.4 ± 0.05
pCO_2 torr	50	45 ± 7	$LMPCO_2$ = 41	45 ± 3
pO_2 torr	—	—	—	30 ± 3
Oxygen Saturation %	65	65 ± 4	65	60 ± 2

The condition of venous blood plays a dominant role in the evaluation of oxygenators. Because of the non-linearity of the oxygen dissociation curve, factors such as pH, pCO_2, and temperature greatly influence the results. Quantitative evaluation of oxygenators calls for stringent control of blood parameters at the inlet of the oxygenator. Table 1 summarizes the ideal input conditions proposed by various groups.

Materials and Methods

In contrast to the conventional systems, the present system makes use of the test oxygenator as deoxygenator and oxygenator sequentially. The modified circuit shown in Figure 2 consists of a single test oxygenator. Two blood pumps, two reservoirs with parallel connections, a heat exchanger and an electromagnetic flow meter complete the circuit. The two pumps are set for near total occlusion and are previously calibrated by timed collection. One pump is used to provide controlled blood flow into the oxygenator and the other for draining the blood from the arterial side. The gas circuit is made up of a set of flow meters for nitrogen, carbon dioxide and oxygen. These flowmeters terminate in a common gas outlet connected to the oxygen manifold of the oxygenator. Reservoirs I & II are continuously flushed with nitrogen to provide an oxygen-free atmosphere.

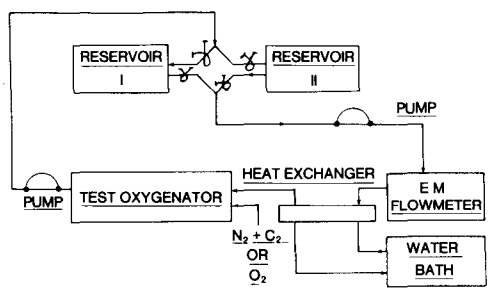

FIGURE. 2. Simplified *in vitro* Test System.

Fresh bovine blood collected under clean, but not sterile conditions was used in all the experiments. Blood was collected in a 3.25% sodium citrate solution (250 ml of the solution/Liter of blood). To this, streptomycin (50 mg/L) and crystalline penicillin (20,000 IU/L) were added. Total hemoglobin was adjusted to 12 ± 0.5 g% by adding normal saline or packed cells. Twenty liters of this blood were primed into the circuit through a standard blood filter. The temperature of blood was brought up to 37°C and maintained within ±0.5°C throughout the experiment. Blood gas parameters and oxygen saturation were checked@ using a blood gas analyzer* and an oximeter.** Correction of pH, if required, was carried out by adding 7.5% sodium bicarbonate solution. Blood gases were adjusted to the optimum value (Refer to Table II) by passing blood through the oxygenator and bubbling nitrogen, carbon dioxide and oxygen as required.

For starting the oxygenation cycle, the venous input pump was stopped and all the blood in the oxygenator was drained into the reservoir II. The clamps on the two lines were changed over to the alternate set of lines. Alternate position of the clamps is shown in Figure 2 as dotted line. The supply of N_2 and CO_2 was discontinued and the required flow of oxygen was present on the flow meter. After a lapse of about one minute, by which time the N_2 and CO_2 were completely flushed out of the gas circuit, the venous pump was started and set for the required blood flow. The oxygenated blood was pumped back from the oxygenator into the reservoir I. After an initial delay of about one minute venous and arterial samples were taken at periodic intervals and blood gas parameters were checked. The oxygen-

@ Continuous monitoring and optimal control of the parameters is better achieved using in-line blood gas analyzers. However in the present work only a discrete analyzer has been used.

* Radiometer BGA 3 blood gas analyzer.

** American Optical Micro Oximeter.

TABLE II
Range of Venous Blood Values Obtained in a Series of Ten Experiments

Hemoglobin	g%	12–13
Hematocrit	%	—
Temperature	°C	37 ± 0.5
pH	—	7.340–7.375
pCO_2	torr (Kpa)	43–49 (5.72–6.52)
pO_2	torr (Kpa)	—
O_2 saturation	%	62–65

ation cycle was terminated when the blood supply was exhausted. Likewise deoxygenation was carried out by replacing O_2 with N_2 and CO_2, the percentage of CO_2 depending upon the pCO_2 value of the oxygenated blood. Deoxygenation was continued until the required blood parameters were obtained. The same procedure was repeated for different blood flow rates.

Results

Table II gives the range of venous blood parameters obtained in a series of ten experiments. The deoxygenation time varied from 15 to 20 minutes depending upon the pO_2 value of the arterialized blood.

Figure 3 illustrates the variation of pO_2 with time at different flow rates. As can be seen, pO_2 values stabilize within the first two minutes and remain steady thereafter. Table III establishes the consistency of the results. In the system described, the oxygenation cycle lasts from 10 to 15 minutes at a low flow of 1 to 2 LPM. However, at high blood flows (5 LPM) the observation period is limited to 4 minutes.

In order to check the validity of this technique especially at high blood flow rates (5 LPM) three experiments were conducted using 80 liters of blood. Fig.

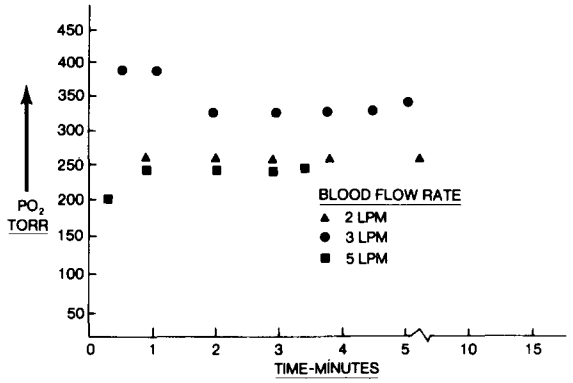

FIGURE. 3. Short term performance of a typical oxygenator at different blood flow rates.

4 gives the results of this study. These results indicate that even at high flow rates (5 LPM) steady state is reached in less than 2 minutes. Thus the readings obtained at 4 minutes can be considered to be truly indicative of the steady state performance of the oxygenator.

Discussion

The closed loop system makes use of continuous deoxygenation and oxygenation. It is necessary to achieve steady state conditions of blood flow, gas flows and blood gas parameters before measurements can be taken. Control of the blood gas parameters of both venous and arterial blood calls for precise control of gas and blood flows. It has also been reported that the percentage O_2 saturation and pO_2 of venous blood tend to rise at high blood flow rates. Since more than one oxygenator is involved, the blood trauma caused by the test oxygenator cannot be directly evaluated. Our experience has also shown that high gas flows are often

TABLE III
Data Obtained During an Oxygenation Cycle Chosen at Random at a Blood Flow of 2 LPM

Time (Minutes)	Venous				Arterial			
	pH	pCO_2	pO_2	O_2 sat.	pH	pCO_2	pO_2	O_2 sat.
0.00								
1.00	7.363	42.6	33	65	7.431	34.6	262	97
2.00	7.367	44.9	35	65	7.419	36.6	415	98
3.00					7.417	36.8	393	98
4.00					7.402	38.2	419	98
5.00	7.370	44.1	33	63	7.407	37.5	417	98
10.00	7.367	45.1	31	62	7.406	37.8	414	98
15.00	7.368	44.1	33	63	7.412	37.1	364*	98
20.00	7.370	44.3	35	65	7.413	38.0	424	98
30.00	—	—	—	—	7.406	38.9	404	98

* Decreased pO_2 was due to increased blood flow which was corrected.

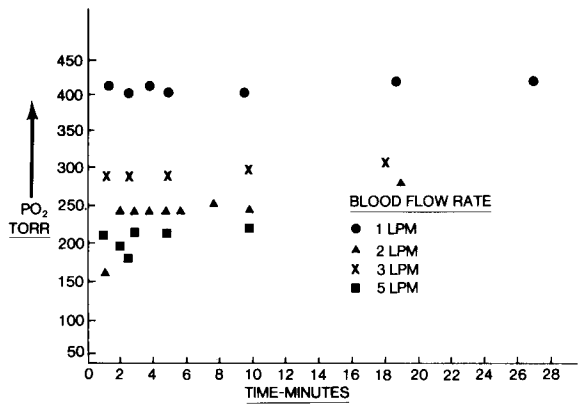

FIGURE. 4. Long duration performance of a typical oxygenator.

necessary in the deoxygenator for sufficient deoxygenation of the blood, especially at high test flows. In the sequential single pass system, in contrast, the deoxygenation and oxygenation are unlinked and accurate control of gas and blood flow is required only for the oxygenation cycle. Apart from providing more stable input conditions, a sequential system, assembled sterilely and using blood collected under sterile conditions, gives a direct indication of the blood trauma produced by the oxygenator. Moreover, as deoxygenation and oxygenation cycles alternate for over six hours, this test also gives a qualitative idea of the defoaming efficiency of the oxygenator over a long period. The same consideration applies to the closed loop system too.

Conclusion

A simplified test set up for *in vitro* evaluation of the oxygenator is presented. Experience has demonstrated the set up to be reliable and simple. No complication has been encountered in the operation of this system. Our experience is however limited to bubble oxygenators and the suitability of this system with appropriate modifications for membrane oxygenators is yet to be studied.

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