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Experimental and Clinical Studies of a Miniaturized Disc Oxygenator for Infants*

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A REVIEW OF THE HEART SPECIMENS OF children who have expired in the Buffalo Children's Hospital from congenital cardiac abnormalities disclosed that about 80 per cent of the infants died within the first 18 months of life. The vast majority of these infants died within the first six months. A careful review of the specimens disclose that 70 per cent are at least theoretically correctable abnormalities. This information has been confirmed

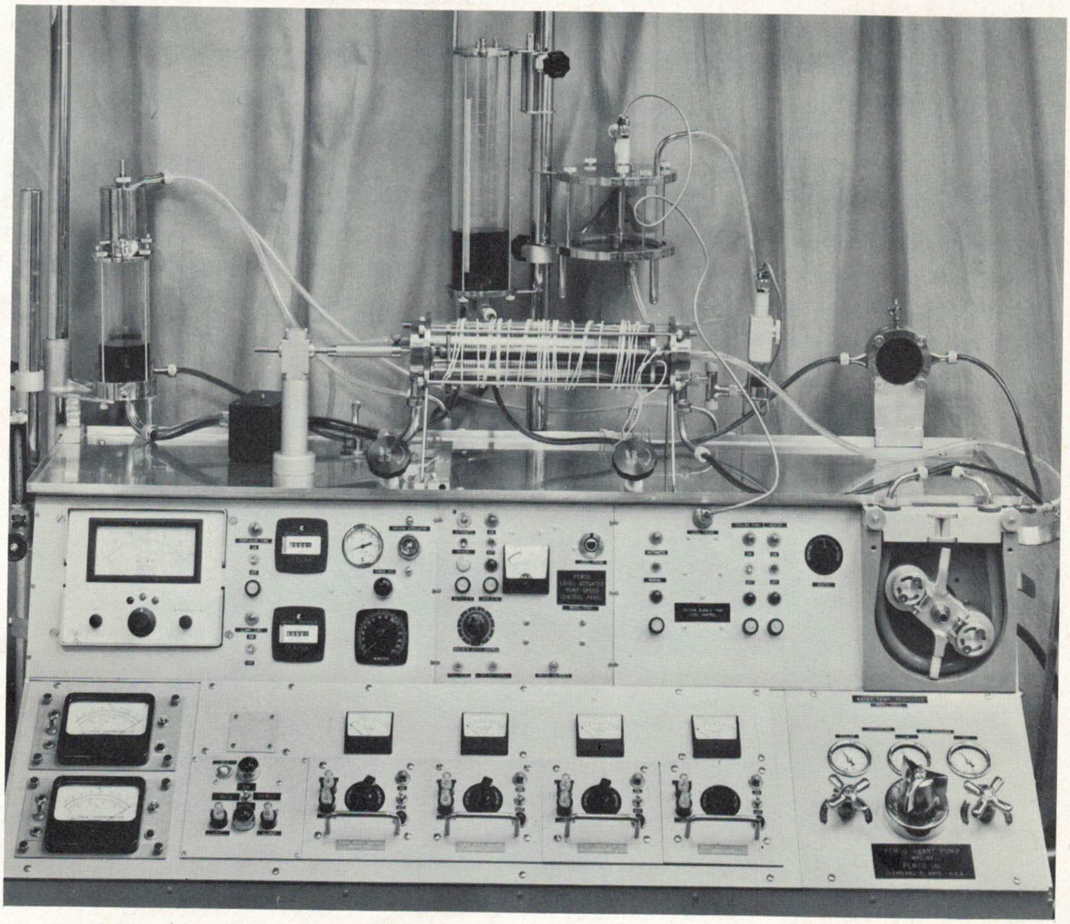

FIGURE 1: Photograph of the oxygenator circuit filled and primed prior to perfusion.

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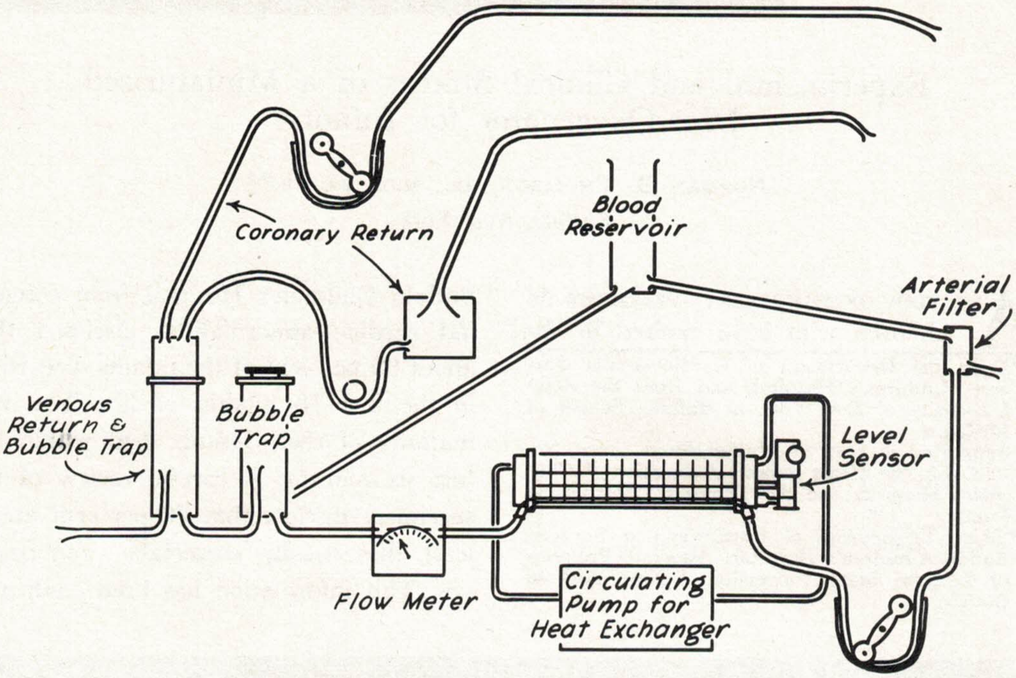

FIGURE 2: Diagrammatic representation of the essential features of the perfusion circuit.

by reviews of pathologic material from other institutions.[6,8,12,13,15,17,19,20]

Because of the inherent difficulties in accurate perfusion in a small child related to control of blood volume, it became readily apparent three years ago that an infant perfusion circuit should be developed. Since we were familiar with the disc oxygenator, we elected to miniaturize and slightly modify the current Kay-Cross disc oxygenator and appropriate bubble trap, venous reservoir, and arterial filter as developed by Gross.[11] The component parts of this perfusion circuit are seen in Fig. 1 and 2.† A transfusion reservoir which is

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†Pemco Company, Cleveland, Ohio.

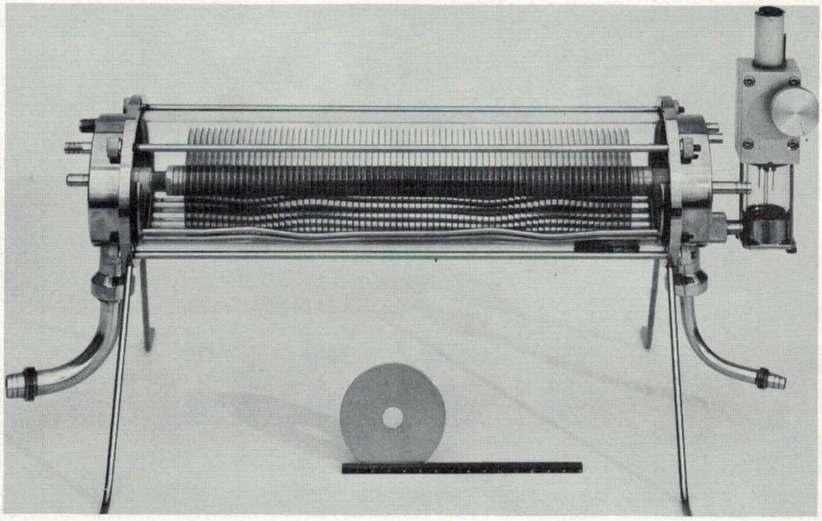

FIGURE 3: Photograph of the infant oxygenator. Note the intraoxygenator heat exchanger of the Gebauer type. The disc is 6.9 mm. in diameter, and this particular oxygenator is 37 cm. long.

calibrated in 10 ml. increments is incorporated in this circuit. This allows one either to transfuse small quantities or to take small quantities of blood from the perfusion circuit in order to maintain the flow rate at a desired level. Venous return is by siphon drainage. A level sensing probe in the oxygenator functions through a feedback servo-mechanism to the arterial pump. This directs the arterial pump to return to the patient all blood that comes into the venous end of the oxygenator, thus maintaining a constant pre-set level in the oxygenator. Since the arterial pump automatically returns the venous blood, an accurate flowmeter is an essential part of this arrangement. Any flow measurement that necessitates stopping the venous return cannot be used. We have incorporated into the venous return line an electromagnetic flowmeter which we have found dependable and accurate.††

In order to utilize such a system for a patient, it would be necessary to know the capabilities of the oxygenator to produce gas exchange. If the amount of oxygen added per disc per minute were known, one might calculate the number of discs necessary to supply the amount of oxygen required by an infant under anesthesia.

The discs (Fig. 3) are flat, stainless steel discs of 0.5 mm. thickness, 66 mm. diameter. The oxygenator chamber is 79 mm. in diameter and may be made to any appropriate length. The priming volume, which includes the volume to fill the 37 cm. long oxygenator and all appropriate tubing including coronary return lines, as well as a sufficiency volume in the transfusion reservoir to complete an operative procedure, is 1200 ml. The presentation of the study of this oxygenator is divided into three phases.

PHASE I

In this portion of the study of the oxygenator, an experimental model was devised (Fig. 4). The small infant oxygenator was coupled in series to a large oxygenator functioning as a deoxygenator. Two sizes of the infant oxygenator were used; a 34 cm. long oxygenator which accommodates 74 discs, and a 15 cm. long oxygenator which accommodates 22 discs. The deoxygenator was perfused with a gas mixture of nitrogen, oxygen, and carbon

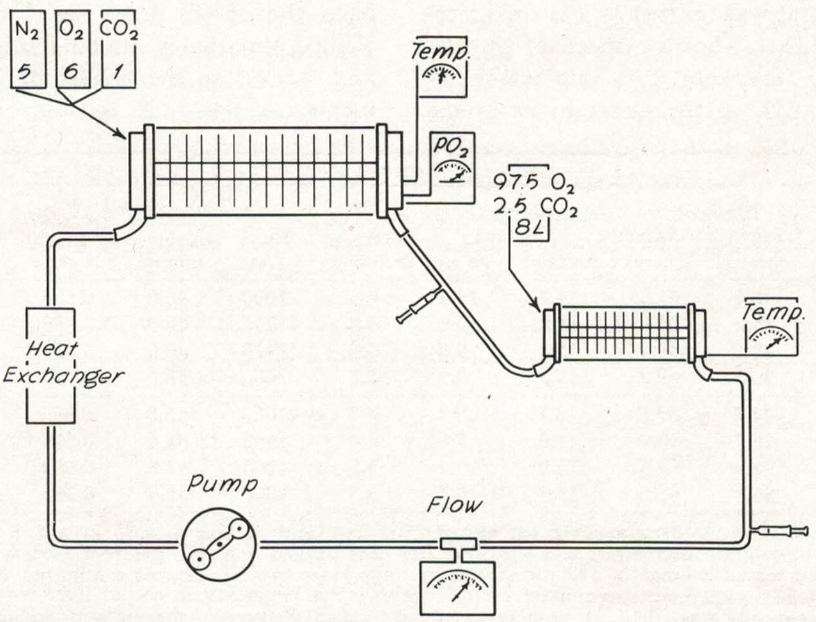

FIGURE 4: Diagram of the experimental model used in phase 1. The larger oxygenator functions as a deoxygenator. Blood samples then may be taken from the venous or arterial side of the infant oxygenator for appropriate analysis.

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††Medicon Company, Model 3000

TABLE 1

Deoxygenator				Miniaturized Oxygenator							
Flow ml./min.	Temp. °C	V. pO_2	RPM disc	pH		CO_2 mEq/L.		pCO_2		Plasma Hgb. mg./100ml.	Hematocrit
				Art.	Ven.	Art.	Ven.	Art.	Ven.		
1400	37.0	65	100	7.39	7.38	26.2	27.9	41.9	43.8	17.0	39.5
1600	37.0	60	100	7.34	7.33	29.0	29.6	50.2	51.2	23.0	39.5
1800	36.5	50	100	7.31	7.31	28.2	29.4	51.3	53.5	39.0	39.5
2000	37.0	50	100	7.30	7.30	29.1	30.2	54.8	56.9	53.0	39.0
2000	37.5	55	120	7.30	7.29	29.4	29.9	55.4	57.4	75.0	39.0
1800	37.5	50	120	7.29	7.28	29.5	30.1	56.4	58.8	81.0	39.0
1600	37.5	55	120	7.29	7.29	28.4	29.6	54.4	57.8	93.0	39.0
1400	37.5	55	120	7.27	7.28	28.0	28.8	55.4	56.1	101.0	39.0

Gas mixture used in the deoxygenator was nitrogen, oxygen, and carbon dioxide in a 5:6:1 ratio. Gas mixture in the miniaturized oxygenator was 97½ per cent oxygen and 2½ per cent carbon dioxide. Experiments ran for an average of 160 minutes at a temperature of 37½ degrees centigrade. Plasma hemoglobin rose 0.64 mg. per cent per minute.

The oxygen capacity was 16.48 ml. A 20 per cent increase in the rpm of the miniaturized oxygenator resulted in an increase in the amount of oxygen added to the blood per minute, very close to a theoretical calculation, if one assumes there is a linear relationship between disc speed and the amount of oxygen added.

dioxide in a ratio of 5:6:1. A Clark pO_2 electrode in the outflow portion of the deoxygenator monitored the pO_2 of the blood. Temperature was maintained at normal thermic levels utilizing a heat exchanger. Flow rate was measured with the electromagnetic flowmeter and recorded. Compatible cross-matched, heparinized human blood was obtained and used to prime the circuit. Because the pH of the 24 hour donor blood is lower than normal, the pH of this circuit was titrated to a normal level utilizing Tris.‡ The disc speed of the deoxygenator was kept at a rate which allowed the pO_2 at the outlet to be in the range of 50 to 60 mm. of Mercury. The disc speed of the infant oxygenator was maintained for a period of ten minutes before arterial and venous samples were obtained. These samples were then analyzed in the Van Slyke apparatus for oxygen and carbon dioxide. PH was measured in the Astrup pH meter, plasma hemoglobin by a modification of the benzine method, hemoglobin and hematocrit by the microcapillary techniques, and pCO_2 was calculated from the above data. Serial experiments yielded remarkably similar results. Tables 1 and 2 disclose the results of five experiments.

TABLE 2

Disc Speed RPM	Per Cent Oxygen Saturation		Oxygen Content		Art.-Ven. Oxygen Difference	Flow Rate	ml. oxygen/ minute	ml. oxygen/ disc/ minute	Average ml. O_2/min./ disc.
	Arterial	Venous	Arterial	Venous					
100	98.4	61.5	14.7	10.2	4.5	1000	45.0	0.625	0.690
	85.2	60.8	14.0	10.0	4.0	1200	48.0	0.666	
	82.3	60.4	13.5	9.9	3.6	1400	50.0	0.694	
	80.5	59.2	13.2	9.7	3.5	1600	56.0	0.777	
120	82.4	57.3	13.7	9.4	4.3	1600	68.8	0.955	0.843 O_2 added at 100 rpm + 20%=0.833
	86.5	59.7	14.2	9.8	4.4	1400	61.6	0.855	
	91.4	61.5	15.0	10.2	4.8	1200	57.6	0.800	
	96.8	62.0	15.9	10.4	5.5	1000	55.0	0.764	

Gas mixture used in the deoxygenator was nitrogen, oxygen, and carbon dioxide in a 5:6:1 ratio. Gas mixture in the miniaturized oxygenator was 97½ per cent oxygen and 2½ per cent carbon dioxide. Experiments ran for an average of 160 minutes at a temperature of 37½ degrees centigrade. Plasma hemoglobin rose 0.64 mg. per cent per minute.

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TABLE 3

Disc RPM	pH Arterial	pH Venous	CO_2 Arterial	CO_2 Venous	O_2 Cap	O_2 Cont. Arterial	O_2 Cont. Venous	O_2 Sat. Arterial	O_2 Sat. Venous	O_2 AV	ml. O_2/ min.
100	7.42	7.37	18.95	19.83	16.14	9.61	5.93	59.5	36.7	3.68	.493
140	7.39	7.33	17.70	19.56	16.14	10.79	5.48	66.6	33.8	5.31	.717

The average results of perfusion of five mongrel dogs with a disc speed of 100, and five with a disc speed of 140. One hundred per cent oxygen was used in the oxygenator. Normal temperature was maintained. PH was maintained in the normal range by using Tris.

PHASE II

Having determined the capabilities of the discs to add oxygen and eliminate carbon dioxide in this ideal in vitro experiment where hemoglobin pH, CO_2, and temperature could be readily controlled, we proceeded to evaluate the same phenomenon in the experimental animal.

Male and female mongrel dogs weighing from 3 to 30 kg. were perfused at normal thermia. The same studies performed in Phase I were carried out. The result of ten such experiments are shown in Table 3.

We were interested in disclosing any difference in CO_2 washout by using 100 per cent ~~carbon dioxide~~ O_2 in the oxygenator. Perfusions were performed in which the 100 per cent oxygen was used for 30 minutes and the 97 per cent oxygen—2½ per cent carbon dioxide mixture for 30 minutes while in five other experiments, the oxygen-carbon dioxide mixture was used for the first 30 minutes, and 100 per cent oxygen for the last 30 minutes. There seemed to be no difference in the results produced by the sequence of gas mixture shown in Table 4. These studies were also designed to test oxygenation capabilities. Consequently, the animals selected were too large to allow the oxygenator to provide for normal oxygen consumptions. The anoxia resulting produced a metabolic acidosis, of course, which is reflected in the CO_2, pH, and buffered base levels.

PHASE III

Having determined the efficiency of this oxygenator in the experimental laboratory, it was then utilized clinically. The same studies obtained in Phase I were then obtained during perfusions of patients. Detailed data were obtained on all patients.

Data obtained during perfusion of the two largest patients for which this apparatus have been used is disclosed in Table 5. The smallest patient for which this apparatus has been used successfully was a 3.7 kg. infant with a body surface of 0.22 M^2 while total anamalous pulmonary venous return was corrected. Since we are primarily interested in how large a patient we can perfuse with this apparatus, only this material is presented. The patient who weighed 9.08 kg. with surface area of 0.34 M^2 was perfused for 73 minutes while endocardial fibroelastosis was decorticated from the interior of the left ventricle. The patient weighing 10.8 kg. with body surface area of 0.36 M^2, was perfused for 125

TABLE 4

		pH	Plasma CO_2 mEq/L.	pCO_2	O_2 Cap.	O_2 Cont.	Per Cent Sat.	A-V	Flow	ml. O_2 d/min.
100% O_2	A	7.33	14.00	25.7	12.84	8.98	70	3.98	1050	0.571
	V	7.27	15.57	33.5		5.00	38.9			
97.5% O_2	A	7.25	15.81	35.4	12.84	9.50	74	3.69	1050	0.531
2.5% O_2	V	7.17	17.00	44.7		5.81	45.2			

Summary of the mean results of five experiments using 100 per cent oxygen and five experiments using 97½ per cent oxygen; 2½ per cent carbon dioxide in the oxygenator. The effect of even small percentage of carbon dioxide in helping to maintain normal arterial pCO_2 is demonstrated. Five per cent ~~oxygen~~ CO_2 and 95 per cent ~~carbon dioxide~~ O_2 is used in perfusions where a temperature below 25 degrees centigrade is maintained.

minutes while a Mustard procedure was carried out to correct a transposition of the great vessels.

DISCUSSION

In the in vitro experiments, flow rates were designed to exceed the capabilities of the miniaturized oxygenator. It is necessary to be certain that the oxygenator is functioning at its maximum capacity. If blood leaving the infant oxygenator is fully saturated it is then impossible to calculate the millimeters of oxygen which might be added by each disc in this infant circuit. By keeping the blood in the outlet unsaturated, we know that the discs are adding the maximum amount possible under those circumstances. The well known effects of varying carbon dioxide, pH, and temperature upon the oxygen dissociation curve, as well as the effects of oxygenation in relation to hemoglobin, were controlled in this experiment.[4,9,10,14,16] The experimental studies utilizing the 37 cm. or 15 cm. long oxygenator are identical. We had thought originally that changes in size of the oxygenator might affect the ability of each disc to add oxygen or eliminate carbon dioxide. This, however, is not borne out by the experimental studies. The amount of oxygen added per disc at 100 rpm. as compared to 120 rpm. theoretically might show an increase by 20 per cent. Table 2 shows that the theoretic calculations are close to the actual measurements. One might reason that the effect of surface area and the time of the blood gas exposure could be increased by increasing the rpm. of the disc. Also, one might reason that a speed of rotation could be attained beyond which additional rates of increasing rpm. would not cause an increase in gas exchange. Additional studies seem to indicate that beyond 140 rpm., the capability of increasing the surface area by increasing the rpm. is no longer possible. The maximum flow achieved through this system because of the various sizes of the orifices and tubing utilized is between 4500 and 5000 ml. per minute. This of course exceeds the required blood flow for patients for whom this system has been designed.

In the second phase of this study in which the experimental animals were per-

TABLE 5

		Temp.	pH	CO_2 mEq/L.	pCO_2	O_2 Cont.	O_2 Sat.	O_2 Consump. ml./min./M^2	O_2 Added ml./d/min.
Wt. 9.85	A	24	7.34	21.08	33	17.01	95.1	61.15	0.31
BSA: 0.34 M^2	V	27	7.24	23.19	46	14.70	82.8		
Age: 18 mos.	A	24	7.36	21.35	32	16.88	96.6	95.82	0.45
Sex: Female	V	28	7.28	22.63	66	13.26	76.1		
Wt.: 10.8	A	34	7.40	20.75	32	16.42	91.0	74.0	0.37
BSA: 0.36 M^2	V	34	7.38	21.63	39	13.88	76.5		
Age: 2½ yr.	A	26	7.30	15.67	31	18.24	100.9	63.0	0.32
Sex: Male	V	26	7.24	15.70	36	15.72	87.0		

Summary of the data obtained on two patients. In the first patient the flow rate was 2.6 liters per meter square per minute. The second patient's flow rate was 2.9 liters per meter square per minute. The amount of oxygen added per minute per disc in these patients may be in error because normal arterial oxygen saturations were obtained. In the second patient, at least 26 degrees centigrade, the plasma was supersaturated with oxygen. Disc speeds used were 120 rpm.

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‡Abbott Laboratories, (hydroxymethyl) aminomethane.

fused, it is interesting to note that the abilities of the miniaturized system to exchange gas is similar to those obtained in the in vitro studies. Again, additional studies indicate that increasing the rpm. over 140 does not necessarily produce a greater gas exchange. The small discs do not produce any foaming or frothing at the rate of 150 rpm. as do the larger discs. This finding is probably related to the difference in the centrifugal force at the periphery of the small discs as compared to the larger discs.

Since the oxygen dissociation curves shift to the left with hypothermia, it has been demonstrated that this curve may be kept in a relatively normal position by controlling the pH in the acid range. On the other hand, an alkalotic pH only exaggerates the shift to the left. Because of this well known phenomenon, it is important to know the ability of the oxygenator to remove carbon dioxide and maintain the pH. The rate of the gas flow through the oxygenator chamber is an important feature in controlling the amount of carbon dioxide eliminated. It is possible to utilize a disc oxygenator with 100 per cent oxygen in the gas chamber if this is kept at a controlled flow rate. However, it is technically easier to have a concentration of carbon dioxide which would not allow pCO_2 to fall below approximately 20 ml. partial pressure. With deeper hypothermia, a 5 per cent CO_2 mixture seems to be indicated.

Since hypothermia is induced in all of our clinical perfusions, we were interested in the function of the oxygenator under hypothermic conditions. Experimental data obtained during hypothermic conditions is noted in Table 5. The pK of carbon dioxide falls with hypothermia and consequently, the pH measurements may be misleading unless changes produced by temperature are realized and the appropriate compensations introduced. The pCO_2 falls during hypothermia because less carbon dioxide is produced. Therefore, it is not difficult to cause respiratory alkalosis by excessive elimination of CO_2 in the oxygenator. The effect of the alkalosis stimulating anaerobic glucose metabolism in the production of lactic acid has been demonstrated, so that one might have, at the termination of the perfusion, a combination of metabolic acidosis as a result of the perfusion, plus a metabolic acidosis as a result of the lactate produced secondary to the alkalosis that was present during the perfusion. The subsequent depression of the buffered base might place a patient in an irreversible situation. Consequently, this data would support the use of carbon dioxide and oxygen mixture for clinical perfusions. The results obtained in both experimental and clinical perfusions indicate that this perfusion circuit will provide adequate gas exchange.

Since arterial samples obtained during clinical perfusions were fully saturated, or even supersaturated with oxygen, the figures disclosed per ml./disc/minute and oxygen consumption may be questioned. Had the arterial blood been less than normally saturated, the figures would be more meaningful, but the price of anoxia is obviously too great to permit us to obtain this data deliberately. The blood gas, acid base, and electrolyte data in the patient who has the longest perfusion with this apparatus, was normal at the termination of the operation. This patient is now well and appears to be cured.

By utilizing a theoretic oxygen consumption for infants and children derived from the work of others, as well as material obtained at our own institution,[5] one can construct a table indicating the total number of discs necessary for infants of various surface areas.[1,5,9,10,14,21] In order to do this, one must know the capabilities of the discs.

These studies indicate that the discs will add 0.5 ml. of oxygen per disc per minute at an rpm. of 120. This is the figure that we use in calculating the number of discs necessary to perfuse patients although the amount added as measured in our experimental studies varied from 0.35 to 0.95 per disc. The 0.5 ml. per disc per minute figure is felt to be the more conservative figure to use. We fashion an oxygenator that will accommodate the calculated number of discs. We also use rpm. of 140 to give an additional safety factor. What effect the corrugating of the discs might have on increasing the surface area, we do not know. The corrugated adult size disc, however, will add 1.75 ml. of oxygen per disc per minute at 100 rpm. as compared to 1.25 ml. with the flat discs. That the method described is reliable for clinical application has been demonstrated by successful perfusions on infants in this institution.

With more and more cardiac centers undertaking perfusions in the small infant, it becomes increasingly important to know the capabilities of the miniaturized oxygenators that are utilized. That this surgery can be performed with an acceptable risk has been demonstrated by Ashmore, Cooley, Kirklin, Sloan, and others.[2,3,6,13,15,17,19,20]

To our knowledge, the information obtained by this study has not been readily available, although numerous surgeons are utilizing miniaturized systems.

SUMMARY

1. A miniaturized disc oxygenator has been manufactured and studied physiologically. The priming volume of this circuit is 1200 ml. This includes the filling of all tubes, as well as the transfusion reservoir allowing one to complete an operative procedure.

2. In vitro studies were made to determine the oxygenating capacity of the miniaturized disc. These studies were then confirmed during experimental perfusions in mongrel dogs.

3. The capacity of the oxygenator to exchange gas adequately was confirmed by studies performed during clinical perfusions, on patients weighing from 3.7 to 10.8 kg. The physiologic data obtained during these perfusions is presented. The studies would indicate that the miniature disc will add 0.5 ml. of oxygen per minute at an rpm. of 120. The disc will also efficiently exchange carbon dioxide.

4. These physiologic studies reported are essential to allow one to assemble an appropriate size oxygenator for clinical perfusions in small infants.

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