CHART I
Typical 50 c.c. - 90 minute Run on 4 Kg. Rabbit

Perfusion time in minutes

	0		30		60		90	
	E.O.	L.O.	E.O.	L.O.	E.O.	L.O.	E.O.	L.O.
pH	7.49	7.51	7.48	7.58	7.39	7.40	7.30	7.40
pCO_2 (mm Hg)	37	36	39	30.5	46.5	44.5	47	36
pO_2 (mm Hg)	49	149	48	175	41	92	45	390

E.O.—Entering Oxygenator
L.O.—Leaving Oxygenator

Small Prime Low-Flow Membrane Oxygenator for Use on Neonates and Small Children

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The results of open heart surgery during the first years of life have been disappointing. The high mortality is frequently considered to be due to the gravity of the intracardiac lesion. It is possible, however, that the high mortality is related in part to the inadequacy of presently available methods of extracorporeal circulation. These may be tolerated by adults provided the procedure does not last too long, but possibly may lead to complications or death in newborns and in infants. By improving the extracorporeal circulation it may thus be possible to improve the results of open heart surgery in infancy.

Since conventional oxygenators are known to cause damage to several blood components (red cells, platelets, plasma proteins, etc.) we postulated that a membrane oxygenator would be more appropriate for open heart surgery in infants. Some of the commercially available membrane oxygenators were investigated in our surgical laboratory and found inadequate for our purposes.

Since 1966 we have been developing a different type of membrane oxygenator which appears promising. The design of this oxygenator was presented to the Annual Meeting of the American Society for Artificial Internal Organs in 1967.[1]

The purpose of the present paper is to describe the design and construction of this oxygenator and to outline some of our experimental investigations related to its use in the laboratory.

Design

The oxygenator consists of numerous fine silicon rubber (0.037″ OD, 0.020″ ID) tubes inserted inside a large tube also of silicon rubber. The larger tube is fashioned as a 'Y' on each end and the fine tubes are introduced via a limb of the Y on either end. The oxygen is flown through the fine tubes and the blood flows through the larger tube around and amongst the smaller tubes. The priming volume of the oxygenator is 45 ml. It is a constant volume low prime apparatus initially designed for total cardiopulmonary bypass. (Fig. 1).

Early Models

The earlier models consisted of as many as 250 fine silicon rubber tubes contained within a tube of 3/4″ ID. The volume of these multiple fine tubes, however, resulted in a rather high resistance to flow.

The efficiency of the oxygenator was assessed by determining the quantity of gas moved across the membrane per minute, i.e., the oxygen transfer rate, at various flow rates.

Assessment of these earlier models revealed that at flow rates of 800 ml. to 1200 ml/minute the average increase in oxygen content was 3.8-4.7 vol. percent. Beagle puppies in the 4 kg. weight range were studied. With flow rates as high as 200 ml./kg. for 30 minutes, oxygenation was adequate, but CO_2 elimination was not. The plasma hemoglobin was recorded as 58 mg. % after one hour of perfusion.

Later Model

In an attempt to provide effective gas transfer at flow rates varying from 50-75 ml/minute, we designed a smaller model with the following specifications: There are 52 fine silastic tubes 14″ long, each tube being 0.037 OD, 0.020 ID contained within a larger tube 3/8″ ID and 1/2″ OD.

Investigation of this model was conducted in rabbits, which ranged in

CHART II

FOUR 2-HOUR PERFUSIONS ON A 4 KG. PUPPY

Normal Runs	90% Nitrogen Runs 10% C_2	0 E.O.	0 L.O.	30 E.O.	30 L.O.	60 E.O.	60 L.O.	90 E.O.	90 L.O.	120 E.O.	120 L.O.
pH		7.33	7.35	7.31	7.35	7.35	7.42	7.37	7.39	7.27	7.30
		31.5									
pCO_2		31.5	36	47	54	43	48	41	39	54	51
pO_2		56	65	59	132	55	132	50	94	45	110
pH		7.35	7.37	7.46	7.47	7.40	7.41	7.05	7.04		
pCO_2		34	32.5	27.5	22	30	25.5	32	32		
pO_2		41.5	110	64	330	47	175	20	47		
	pH	7.45	7.51	7.58	7.62	7.39	7.36				
	pCO_2	22.5	17.5	19	20.5	20.5	22				
	pO_2	21.5	94	22.5	390	22	260				
	pH	7.30	7.33	7.47	7.45	7.42	7.42				
	pCO_2	29	30	27	30	22	21				
	pO_2	21	37	30	68	34	42				

Perfusion time in minutes (0, 30, 60, 90, 120).

weight from 2-4 kg.[2] The anaesthetic agent was sodium pentobarbital, 30 mg/kg. The carotid artery and the contralateral jugular vein were cannulated with a 13-gauge plastic needle. The direction of flow was from artery to vein in order to control flow and also to aleviate the difficulty in getting adequate flow from the veins of these small animals. The pump was situated between the animal and the oxygenator and the blood was pumped through the oxygenator as opposed to being pulled through. Samples were taken before and after passage through the oxygenator.

Oxygen transfer rates were measured at low flow rates. The blood gas tensions were determined with a physiological gas analyzer. (Instrumentation Laboratories). The hemoglobin concentration was determined with a Spencer Hemoglobinometer and the hemoglobin saturation and oxygen content were obtained with the Severinghaus slide rule. A typical 90-minute perfusion on a 3-kg. rabbit is shown in Chart I.

Assessment of Oxygenators of Various Sizes

Ten perfusions were conducted in small beagles ranging from 4 to 12 kg. for purposes of assessing various size oxygenators. (Chart II). In this manner we determined the maximum flow rate and the effective oxygen transfer that each oxygenator was capable of achieving. For example, a 62 tube 1/4″ wide tube oxygenator is capable of effective oxygen transfer with flow rate up to 75 ml. per minute.

This process was carried out with a series of dogs and the results to date have revealed that gas exchange occurred and that carbon dioxide was eliminated, but that after 30 minutes there tended to be a continuous fall-off of O_2 content. This was accompanied by streaming of the blood within the tube which made it necessary to manipulate the oxygenator with some form of squeezing motion to disturb the fine tubes in such a manner as to allow more blood to circulate among them.

We then assessed the effect of a system of "hand-squeezing" (agitation) for 15 minutes compared to a system of "non hand-squeezing" (non-agitation) for a comparable period. The results were monitored by determinations of pH, pCO_2 and pO_2 as shown in Chart III.

(Continued on Page 16)

CHART III

COMPARATIVE RUN ON ANIMAL . . . PARTIAL BYPASS . . . TWIN OXYGENATORS . . . AGITATION BY HAND AND NON-AGITATION

("Squeeze, No-Squeeze Method")

Time		11:00 NA	11:00 A	11:30 NA	11:30 A	12:00 NA	12:00 A	12:30 NA	12:30 A	1:00 NA	1:00 A	1:30 NA	1:30 A
TEMP. °C.		37	37	37	37	37	37	37	37	37	37	37	37
	V	38	42	30	30	36	36	38	38	33	35	42	42
PCO_2 (mm Hg)	A	37	43	27	27	33	33	33	30	34	33	41	43
	V	45	45	51	51	45	45	42	41	38	38	39	38
PO_2	A	51	73	66	360	51	245	51	160	52	155	40	72

N.A.—non-agitation

gasses or the speed of the disc, or using gasses containing CO_2 raises the pCO_2 and lowers the pO_2. These techniques are used in respiratory acidosis or alkalosis.

When metabolic acidosis or alkalosis is indicated drugs are used for correction. If a combination of the two exists, a combination is used for correction. Normally there are 20 cc of oxygen in 100 cc of venous blood (15 volume percent), percent oxygen saturation is approximately 100% in arterial blood and 75% in venous blood of patients with normal circulation.

Conclusion

Based on the comparison of both cc per kilogram and liter per square meter without regard to age, it appears that both systems lean toward underperfusing the thin and over-perfusing the heavy.

Figure No. 5 shows the actual flow range for a given height over a weight range of 100 to 200 pounds in both cc per kg. on L/m^2. The cc per kilogram is based on weight alone without regard to height and is thus consistently the same at each height range. L/m^2 is based on height and weight and thereby shows a difference at each height indicated. The L/m^2 moves upward and the span increases as the height increases over the same weight range. The L/m^2 shows the greatest difference at 200 pounds, indicating more flow to the tall.

Since both scales when compared indicated over-perfusion to the obese and under-perfusion to the thin the L/m^2 seems to show better protection for both obese and thin. Even at that, one can easily notice the difference in the amount the two methods would flow a patient.

At any rate, if the flow is set up using both methods, and given the planned flow a value of 100%, as well as calculating the percentage for the other values, one could easily respond in both systems at the same time giving the percentage, L/m^2, and cc/kg. whatever the flow happened to be. These values are determined ahead of time in our cases. Flow based on cardiac output during cardiac catheterization is not considered a good criterion, because stenosis of the valves, septal defects, etc., tend to lead to cardiac insufficiency.

Summary

Both methods vary somewhat in the total flow one would receive during bypass. Also, if one relied on percentage of planned flow, there would be no correlation from one method to the other unless the flow was determined by both methods. For simplicity of responding to the surgeon, and sometimes to an observer who may be familiar with the other method, and at times when the surgeon would like to know for some reason, we find it helpful to set a comparative flow scale using L/m^2/min., and cc/kg./min. with percentage at each interval. By using a comparative method and noticing that when compared both lean toward a possible need to compensate for the very thin and the obese—it is felt that maybe some arrangement should be made for other variants (e.g., age range).

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Small Prime . . .

Discussion

The importance of the stationary boundary layer of blood next to the membrane, which interferes with the gas exchange, has been recognized by other investigators. Obviously intermittent compression, although it effectively breaks up the boundary layer, is not a practical method. Presently we are designing an apparatus to replace hand-squeezing either mechanically or pneumatically. A prototype of a pneumatic apparatus has been constructed; it exposes the oxygenator to alternating positive and negative pressures within a plastic case.

The agitation must be sufficient to break up the boundary layer in order to improve the oxygen transfer rate, but not so excessive or abrupt as to destroy erythrocytes. Improved design and additional testing are required before the oxygenator can be recommended for clinical use—either for open heart surgery or the management of respiratory distress syndrome.

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