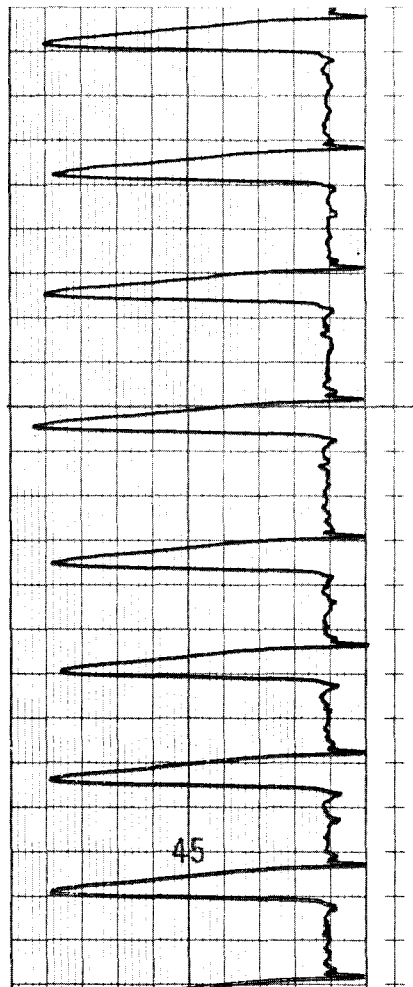


The Landé-Edwards Membrane Oxygenator

Experiences
with 100 patients
during heart
surgery



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INTRODUCTION

Complex coronary artery operations may require prolonged safe total cardiopulmonary support. Cumbersome but effective membrane oxygenators have been used clinically by Kolff¹ since 1953. Kolff¹, Clowes² and later Dobe³ demonstrated that membrane oxygenators cause less damage to blood than bubbling and filming types and therefore seemed more suitable for prolonged use in patients. The crucial difference between bubbling and membrane devices appears to be the absence of direct contact between blood and gas in membrane oxygenators which results in fewer physical and chemical stresses on blood in the membrane oxygenator⁴.

Prototypes of a new membrane oxygenator were developed by Lande' and associates⁵. Blood was separated from gas by a thin silicone rubber sheet folded and separated by a grooved plastic wafer. Blood and gas were manifolded into multiple counter-current flow paths 3 cm in length. Further models of the membrane oxygenator were developed. Minimal apparent blood damage in the Lande'-Edwards Membrane Oxygenator was noted *in vitro* at physiological gas tension⁶.

The present three square meter disposable Lande'-Edwards Membrane Oxygenator (Model 5110-3) has been used clinically for emergency prolonged cardiopulmonary bypass⁷. Patients in refractory cardiogenic shock were provided veno-arterial non-pulsatile partial by-pass perfusion at flow rates between 1,000 and 2,000 ml per minute through a single three square meter oxygenator for periods of 9 to 75 hours.

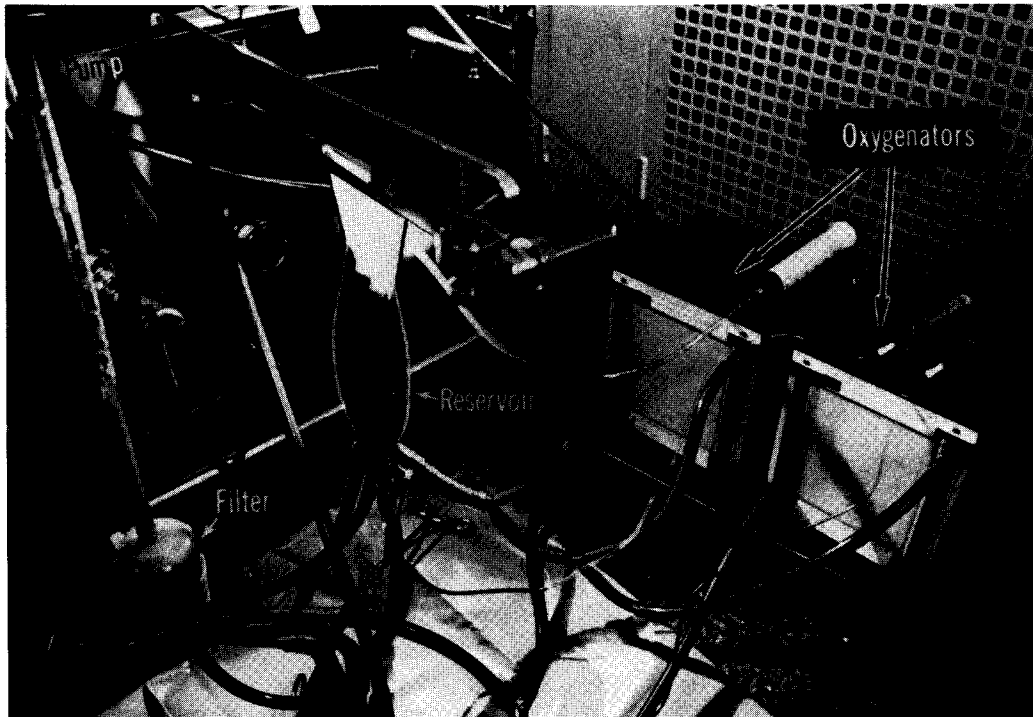
Satisfactory blood pressures were maintained without vasopressor agents. Urine output increased from anuric levels to hourly volumes of 40 to 200 ml. Plasma hemoglobin levels remained below 100 mg indicating minimal destruction of formed blood elements. These encouraging laboratory and clinical results with partial by-pass led us to clinical use of the Lande'-Edwards Membrane Oxygenator for elective operations requiring total cardiopulmonary support. This communication describes the total heart-lung support with the Lande'-Edwards Membrane Oxygenator.

METHOD

Gravity flow directly into the Membrane Oxygenators as first described by Baffes⁸ and modified by us, is now being utilized (Fig. 1). Two 3 meter square Lande'-Edwards Membrane Oxygenators were connected in parallel for patients weighing under 80 Kg (three units for over 80 Kg). The first twenty-three patients were linked to a recirculating circuit with a pump before and after the membrane.⁹ (Fig. 2).

In the gravity circuitry now being used venous blood flowed from the operating table down to and through the membrane oxygenators which were placed near the floor. The blood then flowed into an arterial reservoir which was placed slightly higher than the oxygenators to prevent air embolism. The reservoir must be 30-50 cm below table height to provide sufficient pressure head for adequate blood flow.

An arterial pump took the blood from the reservoir and returned it to the patient's arterial line via a heat ex-



1A—PHOTOGRAPH OF TWO 3-METER SQUARE LANDE'-EDWARDS MEMBRANE OXYGENATORS LINKED FOR GRAVITY CIRCUITRY AND ARTERIAL ROLLER PUMP.

changer. One liter of 5% glucose in water was added to the system for each 3 meter square oxygenator. This dissolved the sodium chloride which was dusted on the membranes during manufacture to prevent the silicone rubber membranes from sticking to one another. Approximately normal saline resulted.

Normal saline or other crystalloid was added to completely fill the system. All air was removed by rapidly rotating the pump while alternately clamping off oxygenators and leaving only one unclamped. Then 12½ gms of salt poor serum albumin per oxygenator was added to coat the membranes and other plastic parts in the circuit. Finally, bottled blood was added via the cardiotomy suction reservoir displacing the priming fluid taking care to not admit any air in the process. A filter with 40 micron pore size removed tiny clots, fat debris and other particulate matter from cardiotomy suction and bottled blood.¹⁰

The speed of the arterial pump was regulated automatically by continuously weighing the blood reservoir contents. Oxygen was transmitted into O₂ inlets at five liters per minute per oxygenator. Since carbon dioxide transfer is the limiting factor in membrane oxygenator perfusion CO₂ gas was only rarely used in the oxygen supply. Maximum blood flow rates were sought and were usually 3000 to 4500 ml/min. (40 to 60 ml/Kg/min.).

Arterial blood pressure was maintained above 60 mmHg by adding blood or Ringer's lactate solution as determined by the hematocrit. Pulmonary ventilation and spontaneous cardiac contractions were continued during cooling to 30°C and during rewarming. Ventilating the lungs permitted maximum carbon dioxide exchange during normothermic partial cardiac support. As described later, the CO₂ exchange was excellent at hypothermia but limited at normothermia when one 3 square meter membrane oxygenator per 40 Kg body weight was used. Comment on the technique is summarized in Table 1.

Evidence for gas exchange, blood damage, and micro air emboli were studied. These parameters included blood gases, platelets, plasma hemoglobin, plasma proteins, fibrinogen, and effect on neurologic, psychiatric, pulmonary and renal function.

Arterial and venous blood gases, hemoglobin, and serum potassium levels were measured hourly during the procedures while off the pump and at a half-hour intervals during by-pass. Formed elements of the blood, including plasma hemoglobin, urine hemoglobin, platelet counts, plasma proteins and fibrinogen levels, were measured at the end of the pump run.

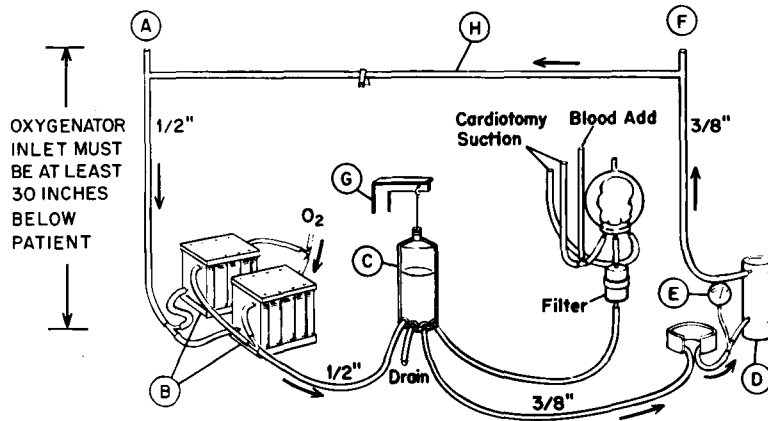
Pre and postoperative Bender-Gestalt tests for mental deterioration and Wechsler Adult Intelligence Tests were compared in alternate patients having similar operations while supported with membrane oxygenator or the Bentley

TABLE I
TECHNIQUE FOR TOTAL CARDIOPULMONARY
SUPPORT USING THE LANDE'-EDWARDS
MEMBRANE OXYGENATOR

- Use one 3M² membrane oxygenator unit per 40 Kg. body weight.
- Maintain heart beat and pulmonary ventilation during cooling and rewarming.
- Pump at maximum flow rates (usually 40-60 ml/Kg/minute).
- Open unused membrane capillaries by periodic flushing every 60 minutes. Shunt entire membrane oxygenator flow through one unit by clamping the blood inlet of the other unit for very short period.
- Maintain the oxygen side of the membrane dry by continuous air flow if the unit is pre-primed for long duration.

LEGEND:

- | | |
|---|--|
| A - Venous Return (1/2") | E - High Pressure Cutoff |
| B - LEMOs Parallel Connection | F - Arterial Line (3/8") |
| C - 1000 cc Venous Reservoir
(level slightly above oxygenator) | G - Pump Speed Control Scale |
| D - Heat Exchanger | H - Shunt for Prime Circulation
and "Sighing" |



GRAVITY SYSTEM FOR TOTAL BYPASS

(AS SUGGESTED BY DR. BAFFES. THIS MODIFICATION USED BY DRS. A.J. LANDE AND R.G. CARLSON)

AUG 1971

1B—TOTAL BY-PASS GRAVITY FLOW SYSTEM USED BY ARNOLD J. LANDE, M.D. AND ROBERT G. CARLSON, M.D. (SIMPLER, PREFERRED METHOD)

bubble oxygenator. Pulmonary function was measured by postoperative blood gases, chest roentgenogram, and ventilation studies. Renal function was monitored by hourly urine output, and postoperative blood urea nitrogen and creatinine levels.

Patient selection initially was limited to the more complicated cases requiring tedious epicardial dissections after previous mammary artery implantations, patients requiring multiple aorto-coronary artery vein grafts, or patients with low cardiac output requiring cannulation and cardiopulmonary support prior to beginning the cardiac operation¹⁰. Later, the membrane oxygenator was used for patients requiring routine open heart operations for congenital heart and acquired valve disease.

RESULTS

100 patients operated by six different surgeons and pumped by five different perfusionists had successful gaseous exchange during perfusions. Details will be presented of first twenty-six consecutive patients who had *successful total cardiopulmonary support* with the Lande'-Edwards Membrane Oxygenator during elective aorto-coronary artery by-pass with saphenous vein grafts performed by R. G. Carlson, M.D. at The New York Hospital-Cornell Medical Center.

Twenty-five of these 26 patients were discharged home improved. One patient, with a successful pump run died on the operating table from acute myocardial failure. The membrane oxygenator provided excellent replacement of cardiopulmonary function with minimal evidence of side effects on other organ systems.

Adequate total support

Excellent exchange of oxygen and carbon dioxide occurred at satisfactory pH levels when the membrane oxygenators

were properly used. During total cardiopulmonary support at hypothermic temperatures of 30°C, the arterial blood gases were excellent as summarized in Fig. 3. During normothermia, in the larger patients hypercapnia gradually occurred unless the lungs were ventilated while the heart was beating. CO₂ diffusion was the limiting factor in normothermic perfusion. This problem was easily surmounted by keeping the heart beating and the lungs ventilated during cooling and rewarming.

During hypothermia, arterial PO₂ ranged from 71 to 625 mmHg, venous PO₂ ranged from 43 to 91 mmHg, arterial pH ranged from 7.24 to 7.51. Oxygen transfer averaged 150 ml/min or 2 ml/min/Kg. Carbon dioxide transfer averaged 130 ml/min or 1.8 ml/min/Kg. See Table II. for example of blood gases in an 80 Kg patient.

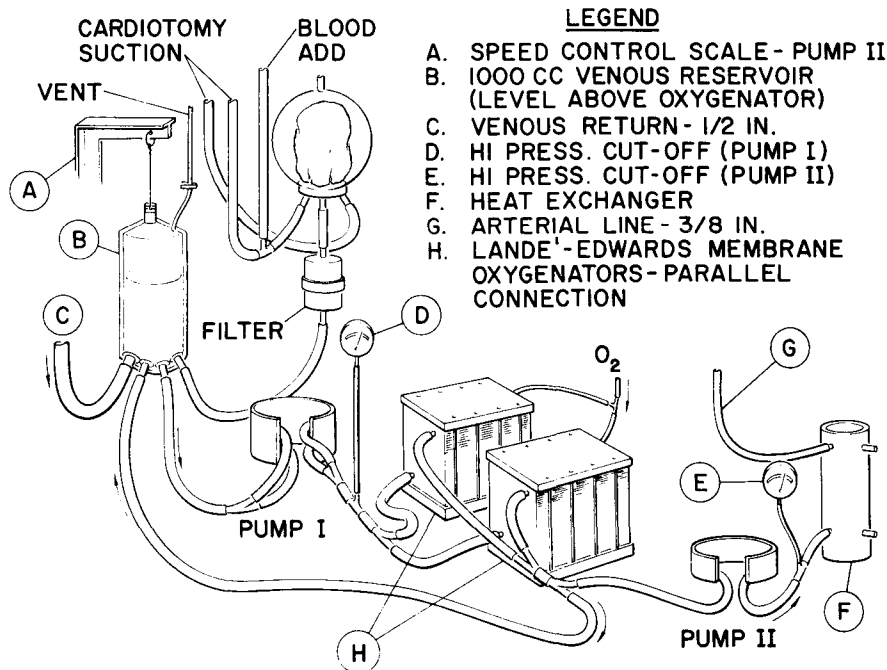
Minimal side effects

Surprisingly few side effects were observed during and after total cardiopulmonary support with the membrane oxygenator. The effects on the blood, heart, lungs, brain, liver and kidneys are summarized in Table III. Samples of blood were removed at the end of the membrane oxygenator pump run. The platelet counts ranged from 69,000 to 200,000/cu. mm, usually about 150,000. The plasma hemoglobin levels remained below 50 mmHg, except when excess cardiomy suctioning occurred the level rose to 250-300 mg%.

The color of the urine, reflecting the plasma hemoglobin levels during and after the pump run, was closely related to the amount of cardiomy suctioning. (Without cardiomy suctioning, the plasma and urine remained yellow during 7½ days of partial body perfusion at 3000 ml/min for a 35 year old female with bilateral pneumonia).

Immediate clotting occurred after administration of protamine to reverse the heparin correlating well with the

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2—TOTAL BY-PASS RECIRCULATION SYSTEM USED BY ARNOLD J. LANDE', M.D. and ROBERT G. CARLSON, M.D. (EARLIER METHOD).

nearly normal levels of fibrinogen and platelets. This immediate clotting occurred after long pump runs and reduced the number of blood transfusions needed. Serum albumin and globulin levels were normal.

Normal cardiac contraction and rhythm, and no unexpected myocardial ischemia were observed after total support with the membrane oxygenator. Most patients walked within 24 hours after operation.

Immediately postoperatively, the lung function was much better than in similar patients supported with the bubble oxygenator.

TABLE II

BLOOD GASES DURING TOTAL AND PARTIAL CARDIOPULMONARY SUPPORT WITH LANDE'-EDWARDS MEMBRANE OXYGENATOR

J. G. 43 yrs.—Double vein by-pass plus
—Mammary artery to Left anterior descending coronary artery.

80 Kg. Two—3 M² Membranes

TIME	Time (min.)	Arterial			Pump arterial flow ml/min.	Hematocrit	Temperature rectal °C
		pH mmHg	PCO ₂ mmHg	PO ₂ mmHg			
Pre-anesthesia		7.40	37	75	—	43	37
Opening chest		7.41	31	190	—	—	37
Total	30	7.41	29	475	3750	27	30
cardio-pulmonary support	60	7.38	40	375	4300	29	30
	90	7.35	39	375	3150	36	30
	120	7.40	41	340	3100	31	30
Partial							
C.P. Support (Heart beating & lungs ventilated)	30	7.39	39	70	2600	29	37
Closing chest		7.44	33	75	—	34	37

1) Postoperative chest roentgenograms showed fewer lung problems of pneumonia, atelectasis, or patchy infiltrates.

2) Postoperative blood gases indicated less frequent and smaller right to left shunts than were commonly seen after prolonged bubble oxygenator pump runs.

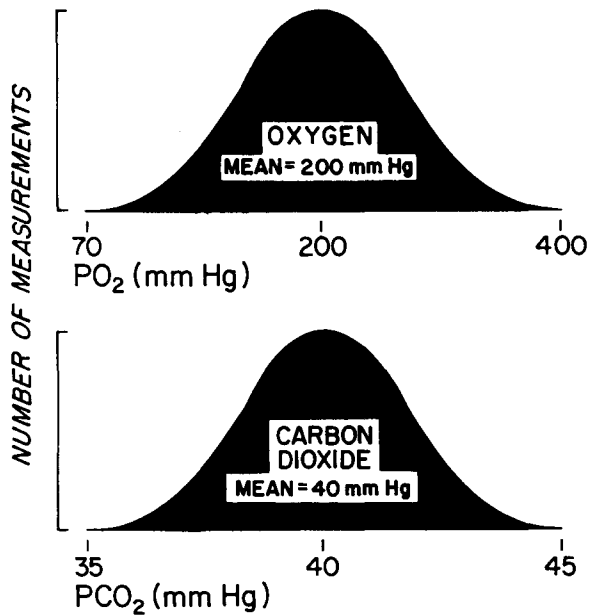
3) Spontaneous ventilation and normal tidal volume allowed early endotracheal extubation.

4) Fewer blood transfusions probably resulted in fewer venous microemboli into the lung.

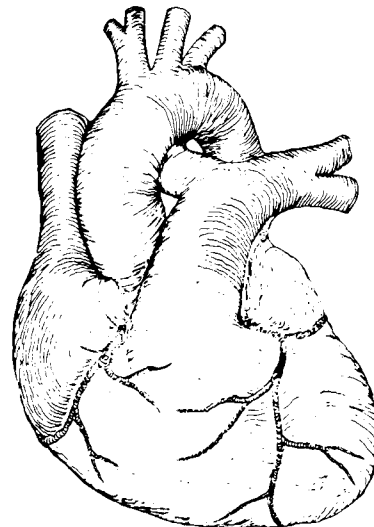
Cerebral function rapidly returned to normal after membrane oxygenator pumping. The effects of bubble versus membrane oxygenators used in alternate cases was studied clinically by Bender-Gestalt tests for mental deterioration and by ultrasonic microemboli counting¹¹.

Much less organic damage occurred after use of the membrane oxygenator by Bender-Gestalt scores. (9% of membrane patients and 40% of bubble patients scores deteriorated more than minus 10 when remeasured 5 days postoperatively). A typical example demonstrating the minimal mental deterioration was a 95 Kg male who was able to discuss philosophy the day after operation needing a 3 hour membrane oxygenator pump run.

Postoperative measurements of hepatocellular and excretory liver functions were unremarkable. Serum bilirubin and prothrombin times remained normal or returned to normal when abnormal preoperatively.



3—ARTERIAL BLOOD GASES DURING TOTAL CARDIO-PULMONARY SUPPORT AT 30°C WITH LANDE'-EDWARDS MEMBRANE OXYGENATOR. (100 PATIENTS).



Glomerular filtration and tubular excretion and secretion were normal or minimally altered postoperatively, excepting one case with hypertensive renal disease and when hemodilution was used for a few prolonged perfusions. A few cases of temporary renal insufficiency occurred during total perfusions of several hours when hemodilution was used. We believe that a gradual decrease in blood volume occurred by crystalloid being lost into the tissues and urine before

adequate blood volume replacement occurred. Since we have avoided hemodilution in the longer pump runs, normal postoperative renal function has occurred. The urine hemoglobin levels were zero unless excess cardiomy suction produced transient plasma hemoglobinuria. Blood urea nitrogen levels measured on the first, third and fifth days were usually below 25 mg% and rarely elevated to 35 to 50 mg%. Urine output during perfusion averaged 500 ml/ hour reflecting good renal blood flow.

TABLE III
ORGAN FUNCTION AFTER USING
THE LANDE'-EDWARDS MEMBRANE OXYGENATOR
FOR CARDIOPULMONARY SUPPORT

CARDIAC	—Electrocardiogram improved after vein bypass. Patients usually walked the day after operation.
BLOOD	—Platelets: 80,000-200,000 cu. mm. Plasma-hemoglobin below 50 mg% (excess cardiomy suctioning resulted in 250-300 mg%) Immediate clotting after neutralizing heparin reduced postoperative blood transfusions.
KIDNEY	—Blood urea nitrogen 12-25 mg% (rarely 35 mg%). Serum creatinine—below 1.2 mg%. Urine output 500 ml/hour during membrane pumping.
BRAIN	—Patient alert enough to "discuss philosophy" the day after operation. Less mental deterioration as measured by Bender-Gestalt testing during membrane compared with bubble oxygenator. (9% of membrane patients versus 40% of bubble patients had post-operative scores worse than preoperative scores minus 10).
LUNG	—Early ambulation and fewer blood transfusions reduced post-operative pneumonia and atelectasis compared with bubble oxygenator.

COMMENT

Gas exchange was influenced by the amount of blood flow through the membrane oxygenator, temperature and weight of the patient, and by supplementing membrane oxygenator carbon dioxide exchange with pulmonary ventilation during partial support while cooling and rewarming the patient.

Maximum venous blood flow was sought; 50 ml/Kg/min. flow was usually adequate. The recirculation circuit used in the first 23 patients was found to be unnecessary. Excellent oxygen and carbon dioxide exchange was obtained in the next 77 patients using the simple gravity flow circuit. One 3 square meter unit per 40 Kg body weight proved adequate.

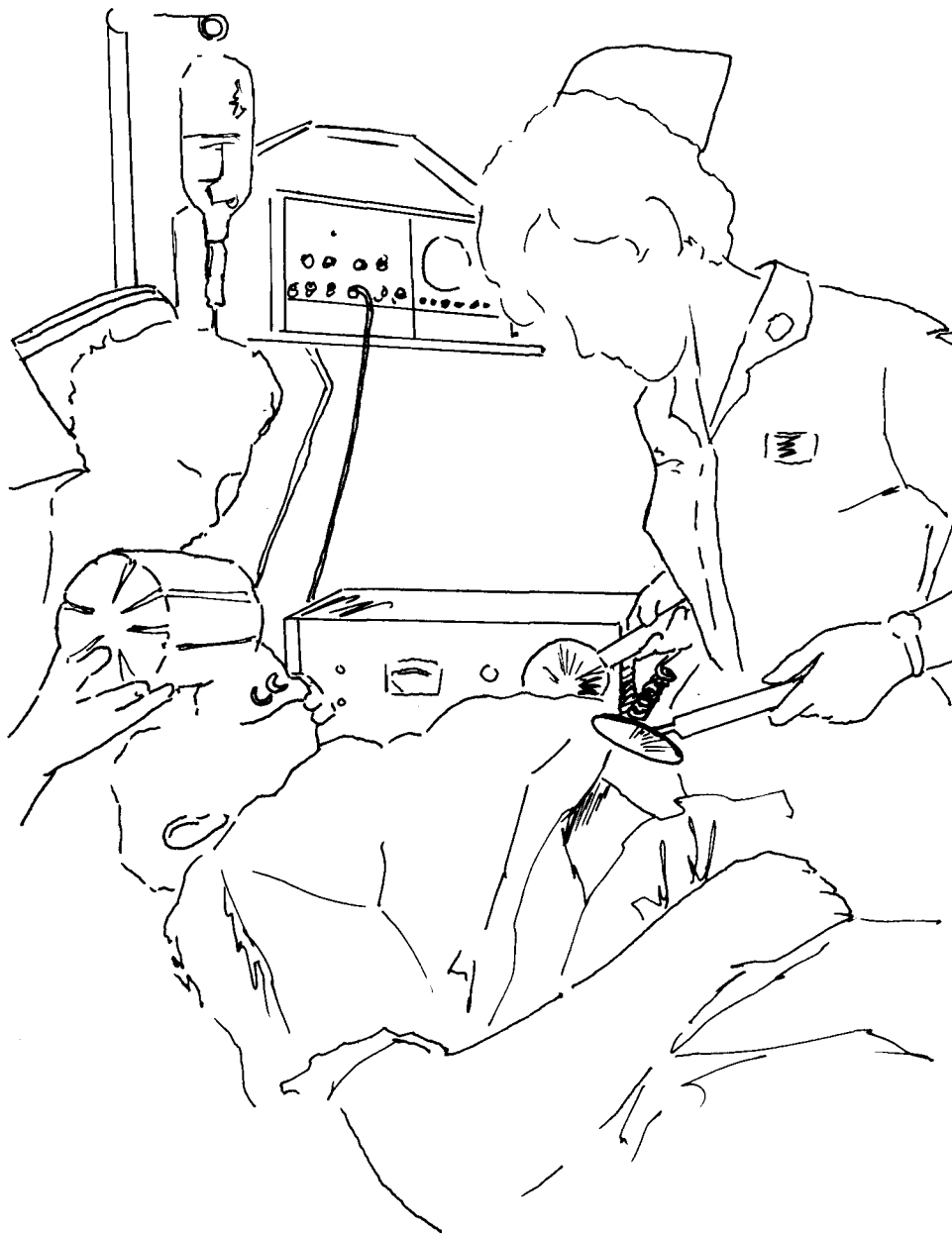
Two patients, 96 and 103 Kg, had satisfactory gas exchange with three 3 square meter units. The arterial PO₂ and 30°C however, was maintained at 93 mmHg for ten minutes using only two units.

Because carbon dioxide exchange is limited, continued pulmonary ventilation and maintenance of cardiac contractions during cooling and rewarming appears advisable in the larger patients. With the membrane oxygenator, the length of pump run is considered to be of less concern than the limited CO₂ exchange at normothermic temperatures. One 90 Kg patient recently perfused with 3 three square meter membranes on gravity required carbogen (2.5% CO₂ and 97.5% O₂) because of hypocarbia.

Periodic high flow perfusion every 60 minutes through each membrane oxygenator unit with the entire venous output appears to avoid "membrane atelectasis" by reopening any unused portions of the oxygenator. Two times in our early experience a membrane oxygenator circuit was filled with saline but without gas flow for 3 days prior to operation. Diffusion of the stagnant saline through the membrane caused oxygenator "atelectasis" and indicated the necessity

of drying the oxygen passages when pre-priming was performed.

Those two patients had poor gas exchange with membrane oxygenators primed for 3 days prior to usage in which no attempt was made to keep the oxygen pathways dry and open. Incidentally, low oxygenation in this case confirmed the "azygos" or low flow principle which permitted safe cross circulation cardiopulmonary support 15 years ago.¹²



SUMMARY

One-hundred patients, 7-103 Kg, received total cardiopulmonary support with the disposable Lande'-Edwards Membrane Oxygenator. Initially the membrane units were used only during complex aorto-coronary artery vein graft operations, reoperations, or when low cardiac output dictated cardiopulmonary support prior to thoracotomy. Later the units were used for routine open-heart surgery. Two 3 meter square Membrane Oxygenators were linked in parallel to a standard roller pump apparatus. (Three 3 meter square membranes for patients 80-103 Kg).

Excellent oxygen and carbon dioxide exchange (2 ml O₂/Kg/min) occurred during hypothermia of 30°C at flows of 50 ml/Kg/min during pump runs of 1-6.5 hours.

Fewer micro gas and particulate emboli were counted in the arterial line of the membrane compared to similar patients with the bubble oxygenator. (1500/min versus 18,000 ultrasonic counts/min). Sonar counts correlated well with the measurements of mental deterioration by Bender-Gestalt visual motor tests. Preoperative scores compared

with scores 5 days postoperatively in 28 alternate patients indicated deterioration of postoperative scores to more than minus 10 in only 9% of patients with membrane, but 40% of patients with the bubble oxygenator.

Minimal blood damage was evidenced by platelet counts up to 200,000/ml, plasma hemoglobin below 50 mg%, with yellow urine unless excess cardiotomy suctioning occurred, and with fewer postoperative fresh blood and total blood transfusions.

Immediate awakening and ambulation in the hallway within 24 hours probably were a consequence of fewer *micro emboli* and fewer blood transfusions. This reduced cerebral and pulmonary complications and permitted earlier hospital discharge compared with similar patients supported with the bubble oxygenator.

The *simplicity* of this membrane oxygenator was demonstrated by its successful use by six different surgeons and five different pump perfusionists.

Its *safety* was demonstrated in the first 26 consecutive patients who had successful total perfusion during complex aorto-coronary vein graft operations. All but one patient were discharged home improved. One patient with successful perfusion died in the operating room from myocardial failure.

The *absence of direct blood-gas interface in the membrane oxygenator* allowed safer prolonged total cardiopulmonary support in our hands compared with the bubble oxygenator.

CONCLUSION

The Lande'-Edwards Membrane Oxygenator provided safe, adequate exchange of oxygen and carbon dioxide during elective total cardiopulmonary support for more than 6 hours and partial support for more than 7 days.

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