

IN VITRO AND CLINICAL STUDIES OF FLUID REMOVAL WITH THE KIIL DIALYZER AND SUBATMOSPHERIC-PRESSURE DIALYSATE CIRCUIT

MASAKATSU SHIBAGAKI, M.D.,* and WILLEM J. KOLFF, M.D.

Department of Artificial Organs

WHEN blood passes through an artificial kidney, a pressure gradient is exerted across the dialyzing membrane. As a consequence, plasma water is removed by ultrafiltration. During the next circuit of the blood through the body, edema fluid replaces the loss of plasma water until it in turn is removed in the artificial kidney. Fluid removal through ultrafiltration by an artificial kidney may be lifesaving for a patient with acute pulmonary edema,^{1, 2} or with increased intracranial pressure.³ Patients desperately ill and cyanotic from pulmonary edema are almost miraculously improved by this fluid removal. An hour and a half of ultrafiltration with an artificial kidney may improve the clinical air hunger so much that a patient may be taken out of an oxygen tent. If the patient can survive for an hour and a half after the onset of dialysis, he probably will live. In the treatment of patients with chronic renal failure, fluid removal by ultrafiltration is necessary for the management of hypertension and the avoidance of otherwise refractory edema.^{1, 2} In many patients who are dependent for life on the artificial kidney, the blood pressure can be controlled at will by varying the total body water and sodium. These patients must be on a salt-restricted diet. When they have no urinary output, they depend for the removal of water and sodium on the artificial kidney. Because excessive removal of body fluid may result in complications such as hypotension or weakness, one should be able to predetermine the amount of ultrafiltration that should take place during each dialysis.

This paper reports the in vitro study undertaken to predetermine the amount of ultrafiltration obtained with a two-layer parallel-flow Kiil dialyzer.⁴ These results were tested in clinical application to obtain a high rate of ultrafiltration in a simple manner; a pump was placed in the outflow tube of the dialysate circuit, to create subatmospheric pressure in the dialysate compartment. This increased a pressure gradient across the dialysis membrane. The amount of ultrafiltration was also found to be related to dialysate temperature but not to the blood flow rate. Variation in dextrose content, which can increase or decrease the rate of ultrafiltration, was not employed in this study.

*Fellow in the Department of Artificial Organs.

This study was supported by a grant from The John A. Hartford Foundation, Inc., to The Cleveland Clinic Foundation, for dialysis in the treatment of patients with chronic renal failure.

Material and Method

A two-layer parallel-flow Kiil dialyzer* was used. A commercially available pump† was placed in the outflow line of the rinsing fluid (Fig. 1). Rinsing fluid was sucked from the Quinton dialysis tank* through a flowmeter and through the dialyzer; after passing through the pump it could be returned to the tank (Fig. 1) or it could be discarded. The flow of the rinsing fluid was controlled by a screw

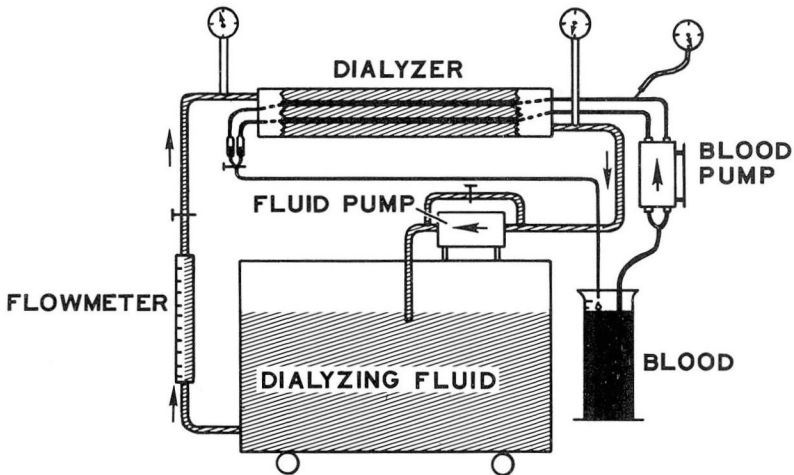


Fig. 1. Two-layer Kiil dialyzer with subatmospheric-pressure dialysate circuit. Sigmamotor pump circulates 'blood' from graduate cylinder through the dialyzer and sends it back to the cylinder. A fluid pump (Hypro Flex) sucks dialysate from the tank through flowmeter and dialyzer, thus exerting subatmospheric pressure on the dialysate compartment. Subatmospheric pressure can be regulated by clamps on bypass around the pump.

clamp on the bypass tubing around the pump. The negative pressure was controlled by the screw clamp on the inflow line. Inflow and outflow pressures were measured by Tycos manometers connected within rinsing fluid tubing. The dialysate flow rate was set for 2 l. per minute. Blood flow was measured by the so-called racetrack method, using a 1-ml. carbon dioxide bubble that runs through a 50-cm. track of horizontal blood tubing. Pressures on blood inflow and outflow blood tubing were measured with the Tycos manometers.

In vitro study. For the first set of experiments, tap water was used both for rinsing fluid and for 'blood' to eliminate the effect of osmotic pressure. For the other experiments, human bank blood and standard bath solution‡ were used.

Blood was kept in a graduated cylinder and was propelled by a Sigmamotor§

*Sweden Freezer Manufacturing Co., 3401 Seventeenth Avenue, W., Seattle 99, Washington.

†Hypro Flex rotor pump, Hypro Engineering, Inc., 700 39th Avenue, N.E., Minneapolis 21, Minnesota.

‡Standard bath composition: Dextrose, 400 mg. %; Na^+ , 130 mEq./l.; K^+ , 2.7 mEq./l.; Cl^- , 102.6 mEq./l.; HCO_3^- , 35 mEq./l.; Ca^{++} , 3.4 mEq./l.; and Mg^{++} , 1.5 mEq./l.

§Sigmamotor Inc., Middleport, New York.

pump. Blood flow rate was regulated by the speed of the pump, and the inflow pressure was maintained at around 90 mm. of Hg (between 80 and 100 mm.). The amount of ultrafiltration was measured by the reduction of the fluid level in the graduated cylinder in which the blood was held. Three or four experiments of 10-minute periods were carried out under the same conditions, and the average value of hourly ultrafiltration was then calculated. A rate of ultrafiltration was expressed in milliliters per hour per unit of pressure gradient. In the experiment with bank blood, blood volume in the cylinder was kept constant by substituting the amount of ultrafiltrate lost with normal saline every 10 minutes. The possibility of leakage of fluid was checked carefully at the beginning as well as at the end of each experiment. In each set of experiments, two different temperatures for dialyzing solution were used: from 14 to 18 C. for cold solution, and from 35 to 37 C. for warm solution.

Clinical study. Ultrafiltration under various degrees of suction on the rinsing fluid was measured on 15 occasions in three patients. Arterial line pressure was from 50 to 80 mm. of Hg with a less than 10 mm. of Hg drop across the dialyzer. Weight of the patient,* intake, and output were measured during dialysis, and the amount of hourly ultrafiltration was calculated. In all instances, standard bath solution was used and the bath temperature was in the range of 14 to 18 C.

Results

Experiments with tap water. There is linear correlation between filtration across the membrane and the amount of fluid removed by ultrafiltration (*Table 1, Fig. 2*). Changes in the rate of blood flow from 100 to 200 ml. per minute did not influence the rate of ultrafiltration (*Table 1A and B*). The rate of ultrafiltration increased gradually from 2 to 3 ml. per millimeter of Hg pressure gradient per hour with an increase in temperature of dialysate from 16 to 36 C. (*Table 1B and C*). As much as 1200 ml. of ultrafiltrate can be removed per hour, but at least 300 ml. per hour was always removed.

Experiment with human bank blood (*Table 2, Fig. 2*). There was linear correlation between the filtration pressure and the amount of ultrafiltrate. The rate of ultrafiltration with blood in the circuit was less than that in experiments with water, probably because of the colloidal osmotic effect of the blood.

When the suction increased from -100 to -300 mm. of Hg, the rate of ultrafiltration rose from 262 to 722 ml. per hour, at around 17 C. (16 to 18 C.) temperature, but from 390 to 1,082 ml. per hour when warm dialysate (35 to 35.5 C.) was used.

Clinical study (*Table 3 and Fig. 2*). In the clinical trial, there was fair correlation between the amount of fluid removed and the level of subatmospheric pressure. The amount of ultrafiltrate was somewhat smaller than that expected from the in vitro

*Bed scale used: Albert Hubscher, Wissenschaftliche Apparate Labor-Be, Hamburg 22, Germany.

Table 1.—Experiment with tap water for both 'blood' and dialysate

Temperature; 'blood' flow rate	Dialysate pressure,* mm. Hg		Ultrafiltrate, ml./hr.		Rate of ultrafiltration, ml./mm. Hg/hr.	Number of measurements	
	Outflow	Inflow	Average	Range			
A							
Temperature,	{	300	200	751	676-846	2.21	8
14.5 to 18 C.;		250	160-165	651	612-696	2.20	7
'blood' flow rate		200	125-130	526	492-570	2.06	10
100 ml./min.		150	75- 85	429	414-450	2.1	6
		100	40	316	294-324	2.0	6
B							
Temperature,	{	300	200	752	708-816	2.21	9
14 to 17 C.;		250	160	656	600-684	2.22	5
'blood' flow rate,		200	110-120	537	486-600	2.17	11
200 ml./min.		150	75- 80	424	396-438	2.07	5
		100	35- 40	306	276-330	2.0	9
C							
Temperature,	{	300	215	1230	1212-1266	3.54	6
35 to 37 C.;		250	175	1038	1014-1062	3.46	6
'blood' flow rate		200	125-140	925	840-990	3.58	9
100 ml./min.		150	90- 95	678	630-708	3.20	6
		100	45- 50	505	480-522	3.00	6

*Pressure of blood inflow was kept around 90 mm. of Hg; outflow pressure was between 70 and 90 mm. of Hg.

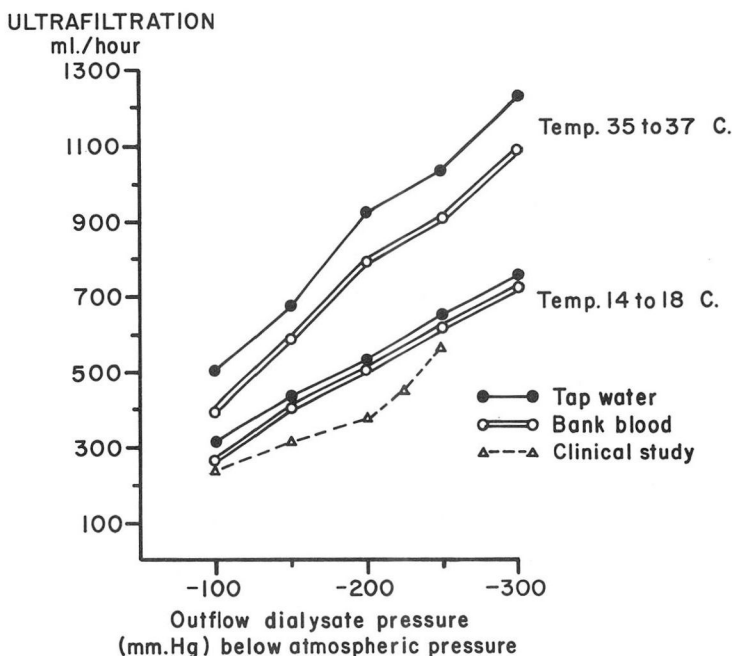


Fig. 2. Graphs showing relationship between ultrafiltration rate and suction.

study, possibly because of lower pressure in the blood compartment. However, the difference was not great. The results of the in vitro study are useful as a guide for the prediction of the amount of fluid to be removed. Changes in blood flow rate did not change the amount of fluid removed by ultrafiltration.

Summary

In vitro study of fluid removal through ultrafiltration was performed with the two-layer Kiil dialyzer with a subatmospheric-pressure circuit. Tap water or human bank blood was used as 'blood' in the experiments. The amount of ultrafiltration increased with the rise of: (1) filtration pressure across the membrane, and (2) dialysate temperature, but did not correlate with blood flow rate. The rate of ultrafiltration was about 2 ml. per millimeter of Hg per hour with low-temperature dialysate (14.0 to 18 C.), and from 3.0 to 3.5 ml. with warm dialysate (35 to 37 C.). More than 1000 ml. of fluid can be removed per hour, but it must be borne in mind that the patient always loses at least 250 ml. of body fluid even when the screw clamp is set for minimal suction.

Table 2.—Experiment with human blood and standard dialysate

Temperature, blood flow rate	Dialysate pressure,* mm. of Hg		Ultrafiltrate, ml./hr.		Rate of ultrafiltration, ml./mm. Hg/hr.	Number of measurements
	Outflow	Inflow	Average	Range		
A Temperature, 16 to 18 C.; blood flow, 100 ml. per minute	300	200	722	702-756	2.1	3
	250	165-170	614	606-630	2.1	3
	200	125	502	498-510	2.0	3
	150	85-90	406	396-426	2.0	3
	100	40	262	246-270	1.04	3
B Temperature, 35.0 to 35.5 C.; blood flow, 100 ml. per minute	300	210	1082	1056-1110	3.1	3
	250	170-175	910	900-930	3.0	3
	200	130	790	780-810	3.0	3
	150	90	588	576-594	2.8	3
	100	45	390	378-402	2.36	3

*Pressure of blood inflow was kept around 90 mm. of Hg; outflow pressure was between 70 and 90 mm. of Hg.

Table 3.—Clinical study on three patients

Temperature; blood flow rate	Dialysate pressure, mm. Hg		Ultrafiltration rate, ml./hr.		Number of measurements
	Outflow	Inflow, range	Average	Range	
Temperature, 14 to 18 C.; blood flow, 80 to 160 ml. per minute	100	60-80	241	233-247	3
	150	100-125	319	290-340	6
	200	100-170	377	338-390	4
Inflow blood pressure was 50 to 80 mm. of Hg with pressure drop of less than 10 mm. of Hg across the dialyzer	225	175	450	—	1
	250	160	560	—	1

The results of the clinical study during 15 dialyses showed fair agreement with those of the in vitro experiment.

The data provided by the in vitro study, make it possible to predict the amount of fluid that may be lost during dialysis. The pressures can be preset to obtain the desired fluid loss, and it is also possible to guard against undesirable complications that are due to excessive fluid loss.

Acknowledgment

The authors herewith acknowledge the technical assistance of Mr. D. van Dura and Mr. H. Tenney.

References

1. Kolff, W. J., and Leonards, J. R.: Reduction of otherwise intractable edema by dialysis or filtration. *Cleveland Clin. Quart.* **21**: 61-71, 1954.
2. Doyle, J. E.; Anthonie, S.; Anthonie, R., and Macneill, A. E.: Ultrafiltration with parallel flow, straight tube blood dialyzer. Introduction and historical review. *New York J. Med.* **62**: 185-202, 1962.
3. Bernard, H. R.; Fischer, H. W., and Bassett, J. W.: Reduction in elevated cerebrospinal fluid pressure by artificial kidney; experiments on acute overhydration in renal insufficiency. *A.M.A. Arch. Surg.* **64**: 365-372, 1952.
4. Cole, J. J.; Quinton, W. E.; Williams, C.; Murray, J. S., and Sherris, J. C.: Pumpless low temperature hemodialysis system. *Tr. Am. Soc. Artif. Int. Organs* **8**: 209-218, 1962.