An Improved Pumpless, Parallel-flow Haemodialyzer* 

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This laboratory previously described a compact haemodialyzer with low flow resistance and low priming volume (Lavender et al, 1968a-1968b). The multilayered dialyzer was manifolde by a technique which did not require tubing inserts or compression seals. It was constructed from cellulose dialysis tubing and inexpensive membrane supports. Moulded entry channels directed blood from a plenum chamber into the cellulose tubes. Blood flowed inside the tubes along the longitudinal axis of the dialyzer. Dialysate flowed outside the tubes countercurrent to blood. Plastic mesh membrane supports separated tubing layers.

In order to simplify construction and to enhance performance, the design has been modified. The moulded blood entry channels have been eliminated and the paths of blood and dialysate have been reversed. Blood flows outside the cellulose tubes and dialysate flows inside the tubes. The membrane supports have been placed inside the tubes.

These design changes have increased effective membrane area, have reduced fabrication costs, and have improved performance. Construction details and results of in vitro and in vivo tests are presented here.

MATERIALS AND METHODS

Membrane support
The plastic screen mesh had filament diameters of 0.25 mm. The filaments were arranged in a diamond patterned lattice. The screen thickness was 0.5 mm. One membrane support was placed within the lumen of each segment of flat cellulose tubing. When layers of support-containing tubes were

*Supported in part by a USPHS Contract from the National Institute of Arthritis and Metabolic Diseases, USPHS Research Grants HE-12965 and HE-12966 from the National Heart Institute, and VA Research Funds from the Hines VA Hospital, Hines, Illinois.
stacked in the dialyzer, blood channel height was determined by membrane sag between support points on the mesh layers. Blood and dialysate were exposed to approximately 67% of the membrane area.

Dialyzer (Figure 1)
Sixteen cm lengths of 4.4 cm wide plastic mesh screen were placed inside 16 cm lengths of 4.5 cm wide cellulose tubing. Sixty-five layers of support-containing tubing were stacked to give an effective membrane area of 5660 cm². The two ends of each layer were coated with a thin film of epoxy resin to give a band approximately 0.75 cm wide. The resin bonded the stacked layers and separated blood from dialysate compartments.

![Diagram of haemodialyzer](attachment:diagram.png)

**Figure 1. Diagram of haemodialyzer**

The stacked unit was placed in a moulded polycarbonate housing which was fitted with tubular entry parts for dialysate and blood. Dialysate entered and left the dialysis tubing lumens via plenum chambers at the two ends of the unit. Blood entered and left from plenum chambers at the sides of the dialyzer. Blood flow was directed perpendicular to the dialysate flow and flowed between layers of dialysis tubes.

The dimensions of the dialyzer were 19 x 5 x 4 cm. The functional part of the unit was 14.5 x 4.5 x 4 cm. The dialyzer weighed 350 grams. A completed dialyzer is shown in Figure 2.

**Protocol**
The longitudinal axis of the dialyzer was oriented vertically. Blood entered near the top and dialysate entered at the bottom. Blood was propelled with a constant speed pump except in pumpless experiments. A constant speed pump drew dialysate through the dialyzer, and a single pass dialysate system was used. Dialysate temperature was maintained constant at 38°C.
Blood and dialysate flows were measured by timed collections in a graduated cylinder. Inflow and outflow blood pressures were monitored, and outflow dialysate pressure was monitored. Pressure in the dialysate compartment was always subatmospheric. A schematic diagram of the testing circuit is shown in Figure 3.

Figure 3. Haemodialyzer testing circuit
For in vitro experiments, a modified Ringer's solution with added creatinine served as blood. Tap water was used for dialysate. For in vivo experiments, standard isosmotic dialysate solution was used. In all studies, blood and dialysate entering and leaving the dialyzer were sampled simultaneously for estimation of dialysance.

In animal experiments, mongrel dogs of 20 to 22 kg body weight were anaesthetized with intravenous pentobarbital sodium. A constant speed pump infused creatinine and urea intravenously. The femoral vessels were cannulated and connected to the dialyzer with silicone rubber tubing.

Ultrafiltration was estimated by collecting filtrate from the overflow of a recirculating dialysate reservoir. In some experiments, ultrafiltration was estimated by the uptake of saline from a graduated cylinder by an open branch of a closed blood circuit. Chemical analyses and calculations were those which have been described previously (Lavender et al, 1968a).

RESULTS

Dialyzer characteristics (Table I)
The effective membrane area was 5660 cm$^2$ in a 65 tube dialyzer. Priming volume at zero pressure, exclusive of blood tubing, was 38 ml. At a transmembrane pressure of 200 mm Hg, dynamic volume averaged 70 ml. Filtration rate for blood was 1.6 ml/min at a transmembrane pressure of 100 mm Hg, and was 6.0 ml/min at a transmembrane pressure of 400 mm Hg. Filtration pressures were generated by negative pressure in the dialysate compartment. The blood channel height averaged 90 microns at zero pressure and 125 microns at 100 mm Hg transmembrane pressure.

<table>
<thead>
<tr>
<th>TABLE I. Dialyzer Characteristics</th>
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<tbody>
<tr>
<td>Dimensions</td>
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<tr>
<td>Weight</td>
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<tr>
<td>Number of Tubes</td>
</tr>
<tr>
<td>Effective Surface Area</td>
</tr>
<tr>
<td>Priming Volume</td>
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<tr>
<td>Dynamic Volume (200 mm Hg)</td>
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<tr>
<td>Filtration Rate:</td>
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<tr>
<td>100 mm Hg</td>
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<tr>
<td>400 mm Hg</td>
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<tr>
<td>Blood Channel Height (average)</td>
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</table>

Transmembrane pressures in excess of 1000 mm Hg did not cause rupture or leak at resin-tubing seals. Blood flow resistance was low. At blood flow of 300 ml/min and dialysate flow of 500 ml/min, pressure drop in the
blood compartment was less than 2 mm Hg for aqueous solutions and less than 5 mm Hg for blood.

In Vitro Tests (Figure 4)
When blood flow was held constant at 312 ml/min, dialysances of creatinine, chloride, and potassium increased progressively as dialysate flow increased. At a dialysate flow of 1.1 ml/min creatinine dialysance was 65 ml/min and potassium dialysance was 85 ml/min.

![Figure 4. Effect of dialysate flow on dialysance in vitro](image)

In Vivo Tests (Figure 5)
When dialysate flow was held constant at 400 ml/min, urea and creatinine dialysances increased progressively as blood flow increased. At a blood flow of 150 ml/min, creatinine and urea dialysances were 53 ml/min and 75 ml/min, respectively. At a blood flow of 600 ml/min, creatinine and urea dialysances were 69 ml/min and 100 ml/min, respectively.

![Figure 5. Effect of blood flow on dialysance in the dog](image)
When conventional shunts were implanted into the femoral artery and vein, blood flow was 324 ml/min in an animal with a mean arterial pressure of 60 mm Hg (Figure 6). At a dialysate flow of 500 ml/min, creatinine and urea dialysances were 70 ml/min and 83 ml/min, respectively. When dialysate flow was increased to 1500 ml/min, creatinine dialysance was 85 ml/min and urea dialysance was 92 ml/min.

Clinical Tests (Table II)
Preliminary clinical tests have given results comparable to those obtained in dogs. Creatinine dialysance ranged from 39 to 55 ml/min at blood flows of 165 to 330 ml/min. Urea dialysance ranged from 51 to 93 ml/min. Filtration rate varied from 2 ml/min to 8.4 ml/min, at transmembrane pressures of 160 to 320 mm Hg.

TABLE II. Clinical Trials of Dialyzer

<table>
<thead>
<tr>
<th>Patient</th>
<th>Blood Flow (ml/min)</th>
<th>Dialysate Flow (ml/min)</th>
<th>Dialysance Creatinine (ml/min)</th>
<th>Dialysance Urea (ml/min)</th>
<th>Pressure (mm Hg)</th>
<th>Filtration Flow (ml/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>165</td>
<td>500</td>
<td>39</td>
<td>51</td>
<td>180</td>
<td>6.6</td>
</tr>
<tr>
<td>2</td>
<td>198</td>
<td>688</td>
<td>55</td>
<td>93</td>
<td>320</td>
<td>7.6</td>
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<tr>
<td>3</td>
<td>288</td>
<td>480</td>
<td>49</td>
<td>73</td>
<td>205</td>
<td>4.7</td>
</tr>
<tr>
<td>4</td>
<td>300</td>
<td>450</td>
<td>53</td>
<td>68</td>
<td>300</td>
<td>8.4</td>
</tr>
<tr>
<td>5</td>
<td>330</td>
<td>500</td>
<td>48</td>
<td>73</td>
<td>160</td>
<td>2.0</td>
</tr>
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Plasma haemoglobin levels were unaffected during dialysis periods of 1 to 6 hours, blood pressure was stable, and no untoward reactions were attributable to the procedure. Clotting did not occur in the dialyzer as shown by a constant pressure drop across the dialyzer and by constancy of dialysance.

DISCUSSION

This dialyzer has several advantages over the dialyzer previously reported by us. The unit is smaller, lighter in weight, and has greater effective membrane area. Priming volume is less than 50% of that observed in the earlier model and ultrafiltration rate has been increased two to threefold. Dialysance is approximately 33% greater for this design than for the earlier design. A further increase of 20% can be anticipated should Cuprophane be substituted for regenerated cellulose tubing.

Limited clinical trials indicate that a 12 hour dialysis should be adequate for the average adult patient. Shorter treatment periods should suffice for infants and small children. The low priming volume and small change in volume with pressure should be advantageous in children and subjects with unstable cardiovascular systems.

The simplicity and compactness of this dialyzer suggest clinical applications other than treatment of chronic renal failure, such as emergency therapy of acute hyperkalaemia and drug intoxication. The relatively high filtration rate and low priming volume may be of value in therapy of refractory oedema states, such as congestive heart failure.

Dialyzers are now being constructed by hand in limited quantities. Work is underway to automate fabrication on machines. A compact, portable dialysate delivery system has been constructed, but not yet evaluated. The principle of this system has been described (Lavender et al, 1968c). Attempts to clean and re-use dialyzers have been unsuccessful, but we are hopeful that this problem can be solved. The objective of this programme is a dialyzer and delivery system which will permit home dialysis by all patients who need therapy, at a cost which is not prohibitive to the average family.

SUMMARY

A newly designed pumpless, multilayered, parallel-flow haemodialyzer is described. The effective membrane area is 5660 cm², and the priming volume is 38 ml. Flow resistance is minimal and ultrafiltration rates are 2 to 8 ml/min. Early clinical trials indicate that a 12 hour dialysis will be adequate for therapy of the average adult patient.

Acknowledgments
The authors are indebted to the following persons for their skilful technical assistance: Mr. Arthur A. Berndt, Mr. Frank Anderson, Miss Theresa Gogol, Mrs. Susan Galinis, Mr. Corinth Hobson, Dr. Jack Pinto, Mr. Lee
Perrin, Mr. Thomas Benham, Mr. Raymond Lukes, Mr. Jay Hoffman, and Mr. N. Colliani.

We thank Mrs. Margaret Thomas, Head Nurse, Haemodialysis, and Mr. Henry Bey, Chief Technician, Haemodialysis and the Haemodialysis staff for their aid in clinical studies.

Cellulose tubing was provided by Mr. James Lloyd, Union Carbide, Incorporated, and Baxter Laboratories, Incorporated supplied the membrane support and blood pumps. Dialysate pumps were supplied by Mr. Stephan Richman of Cole-Parmer, Incorporated.

REFERENCES