Clinical Evaluation of New Haemodialysis Membranes

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New synthetic vinyl copolymer membranes have been prepared and investigated as possible replacements for cellulose membranes in flat plate and coil dialysers (Muir et al., 1970a; Muir et al., 1970b; Muir et al., 1971). These anionic and cationic heat or solvent sealable membranes have been evaluated in vitro for permeability to blood solutes, ultrafiltration rates (UFR) and properties. Clinical evaluation of these copolymer membranes has been concerned with their biocompatibility, solute and water transport characteristics in comparison with Cuprophan PT 150. Animal implant and blood exposure studies show no evidence of biological intolerance and blood clotting studies indicate favourable properties of the anionic and neutral membranes.

A phenomenon occurs which may be akin to the protein polarisation (Henderson et al., 1967) property observed with diafiltration membranes and which has had no adverse effects on the intact animal or solute transport. This effect occurs when blood flows over the new membrane materials and may produce a temporary apparent fall in concentration of several plasma proteins. A single layer AB Gambro dialyser was utilised as a test bed for membrane solute transport and UFR studies. Copolymer UFR, urea and creatinine clearances were significantly improved over those for Cuprophan PT 150. In dialysers with high mass transfer efficiencies Cuprophan PT150 imposes limitations on the minimum area required for clinically acceptable UFR. The use of these novel copolymer membranes can substantially reduce this minimum membrane area while maintaining adequate clinically acceptable mass transfer rates.

EXPERIMENTAL

This communication is concerned primarily with evaluation of membrane biocompatibility and examination of the mechanism of blood component deposition on the surfaces of dialysis membranes. For the investigation
unheparinised dog blood was passed over candidate membrane surfaces in double sheets held together by a test cell in a thin envelope. The test cell circuit is illustrated in Figure 1. The Babb-Grimsrud (Babb & Grimsrud, 1966) test cell consists of two Perspex blocks with nickel foam inserts acting as membrane supports. The two blocks are separated by a polythene gasket and blood ports consist of PVC tubing, sealed by silicone rubber adhesive. The plates are clamped together by screws.

Two test cells were used at each experiment, the test membrane envelope being built in to one cell and a Cuprophan PT 150 membrane envelope as control in to the other cell. Unheparinised blood from the animal’s femoral artery was allowed to flow unpumped into both test cells in parallel, blood flow through each cell being equalised at the commencement of the experiment. The blood was then allowed to return to the femoral vein. At no time was there any air-blood interface, the entire system having been primed with saline at the commencement of the experiment. Blood exposure times at separate experiments were 2, 5, 10, 12 and 28 min. Immediately after these exposure times heparin was introduced into the test cells to prevent further clotting, then both cells were washed for one minute with 0.9 g/100 ml saline, 250 ml being used for each cell. Thereafter, the cells were primed with fixative (glutaraldehyde-buffer solution) for scanning electron microscopy.
<table>
<thead>
<tr>
<th>Blood exposure time (min)</th>
<th>Series 10</th>
<th>Cuprophan</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>0</td>
<td>+</td>
</tr>
<tr>
<td>5</td>
<td>0</td>
<td>++</td>
</tr>
<tr>
<td>10</td>
<td>0</td>
<td>+++</td>
</tr>
<tr>
<td>12</td>
<td>+</td>
<td>+++</td>
</tr>
<tr>
<td>28</td>
<td>+</td>
<td>+++</td>
</tr>
</tbody>
</table>

Grading 0 = No thrombus  
+ = Minimal thrombus  
++ = Patchy thrombus  
+++ = Gross thrombus

After a period of from 1-4h, the cells were dismantled and a coloured photograph taken of the exposed membrane surface prior to rapid air drying or freeze drying. Membrane samples were mounted, coated with gold-palladium then examined in a Cambridge stereoscan electron microscope. Table I gives the results of clot observation on both membranes and Figure 2 shows gross photographs of test cells at 10 min and demonstrates favourable antithrombogenic properties of Series 10 surface (on the righthand side

Figure 2. Cuprophan membrane (left) exposed to unheparinised dog blood for 2 min; series 10 (right) exposed 10 min to unheparinised dog blood
of Figure 2) as opposed to Cuprophan membranes (on the lefthand side of Figure 2). Scanning electron photomicrographs are shown in Figures 3 and 4 and demonstrate differences in the type of clot formation immediately adjacent to the membrane surface, between Cuprophan and Series 10 surfaces. On Cuprophan there is considerable fibrin formation, but little evidence of other protein matrix. Series 10 clot structure seems to consist mainly of protein layer with initially deposited red cells and little fibrin strand formation. The in vitro clotting tube study results are given in Table II. These correspond well with the in vivo flow studies and demonstrate the importance of prewetting hydrophilic surfaces prior to assessing their thrombogenicity as dialysis membranes.

Change in red cell morphology has also been observed by scanning micro-

![Figure 3. Red cell thrombus on Cuprophan surface with fibrin strands. x 1000](image1)

![Figure 4. Red cell thrombus on series 10 surface absence of fibrin strands. Initially deposited protein layer with red cell 'foot prints'. x 950](image2)

**Table II. Results of in vitro whole blood clotting study**

<table>
<thead>
<tr>
<th>Membrane coating</th>
<th>Pre-wetted</th>
<th>Dry</th>
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<tbody>
<tr>
<td>Series 20 Unmodified</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>Modified</td>
<td>9</td>
<td>3</td>
</tr>
<tr>
<td>Series 10 Unmodified</td>
<td>25</td>
<td>13</td>
</tr>
<tr>
<td>Modified</td>
<td>11.5</td>
<td>10</td>
</tr>
<tr>
<td>Strathclyde Silicone</td>
<td>-</td>
<td>12</td>
</tr>
<tr>
<td>Glass Control</td>
<td>-</td>
<td>6.5*</td>
</tr>
</tbody>
</table>

*Base standard
scopic in relation to all the dialysis membranes studied, possible causes being:

(a) prosthetic membrane material effects on the red cell membrane
(b) extracorporeal flow effects
(c) protein denaturation effects
(d) microscopy preparation technique

In order to examine these abnormalities a series of comparative static and flow experiments using Cuprophan, copolymer membranes, glass and aluminium surfaces is underway.

ACKNOWLEDGMENTS

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