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Dialysers and Blood Loss in Regular Dialysis Therapy
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The anaemia of chronic renal failure is seldom completely corrected by regular dialysis treatment (RTD). This anaemia is usually associated with a normochromic, normocytic blood film and is basically due to a decreased rate of erythropoiesis associated with the incomplete correction of the uraemic syndrome afforded by haemodialysis. The anaemia may be augmented and complicated by the development of folic acid deficiency, iron deficiency, and considerable blood losses. Androgen therapy has been advocated as a means of increasing the rate of erythropoiesis (Richardson & Weinstein, 1970; Shaldon et al, 1971; De Palma et al, 1972; Ferrier et al, 1972) but results have not been universally successful (Mayer & Robinson, 1971) and side effects may occur (Richardson & Weinstein, 1970; Shaldon et al, 1971; Ferrier et al, 1972). Folic acid deficiency, resulting from losses across the dialyser, is the simplest of the aetiological factors to deal with (Hampers et al, 1967) and most clinicians are satisfied with replacement therapy using oral folic acid supplements. Achievement of proper iron balance on regular dialysis is a more complex problem. Patients with chronic renal failure not on dialysis have been shown to have both decreased absorption of oral iron and diminished incorporation of iron into erythrocytes (Dubach et al, 1948; Boddy et al, 1970). Thus, patients commencing RTD do so with clearly demonstrable abnormalities in iron metabolism. According to Lawson and his colleagues (1971) these abnormalities are not improved by regular dialysis treatment although Comty et al, (1968) have claimed that increased oral iron absorption may take place after the commencement of RTD in patients who are iron deficient, and Eschbach et al (1967) noted an improvement in the ability to utilise iron with increasing time after beginning RTD. Once on the dialysis programme the patient has a rate of loss of iron from the body significantly greater than normal controls and non-dialysed patients with chronic renal failure (Lawson et al, 1971) and this has been attributed to the volumes of blood lost during haemodialysis (Will et al, 1970; Hocken
& Marwah, 1971; Evans et al, 1967; Wright et al, 1968). Such iron loss is sufficient to cause a fall in the haemoglobin and it would appear to be at least partially remediable; Hocken and Marwah (1971), for example, were able to raise the mean haemoglobin of a group of patients from 5 g to 9 g/100 ml with the use of intravenous iron. The work of Lawson et al (1971), however, would suggest that the administration of either oral or parenteral iron is unlikely to be wholly successful because they clearly demonstrated in their patients, using traces doses of $^{59}$Fe, that the absorption of oral iron remained low and the incorporation of the radioactive iron into the erythrocytes remained subnormal. It is certainly our experience that the use of intravenous iron does not help the majority of patients and may indeed be detrimental by causing haemosiderosis.

The policy of maintaining haemoglobin levels by giving repeated blood transfusions in amounts varying from less than one unit of packed cells to four units per month (Eschbach et al, 1967) is no longer acceptable in RDT patients because of the risks of hepatitis (Jones et al, 1967; Drukker et al, 1968; Brunner et al, 1972; Rosenheim Report, 1972) and because of the possible development of leucocyte antibodies which could jeopardise subsequent renal transplantation (Batchelor, 1969; Brunner et al, 1972). Furthermore, routine transfusion may also be incriminated in the development of haemosiderosis.

Considering these factors, it is obvious that if we hope to maintain a reasonable haemoglobin level more attention must be paid to sources of blood loss; for there is no doubt that haemodalysis causes considerable volumes of blood to be lost over periods of time. Hocken and Marwah (1971) found that a minimum of 1.57 litres of blood were lost per annum because of the residual blood volume in the dialyser (standard two layer Kiil system) and the blood taken from the patient for laboratory investigations and that this figure could rise to 4.62 litres per annum if the high volume of blood sampling during the period of establishment on dialysis were continued. In this editorial we wish to consider the sources of what is equivalent to chronic haemorrhage during dialysis and to discuss the mechanisms responsible so that attempts may be made to minimise them. In this connection we may recollect that a blood loss in excess of 2 - 4 ml per day (730 to 1,460 ml per year) will lead to iron deficiency anaemia in an otherwise normal individual unless iron absorption from the gut is extremely efficient (Moore, 1958).

**SOURCES OF BLOOD LOSS DURING HAEMODIALYSIS**

These may be enumerated as follows:

1. Blood loss from the arteriovenous shunt or fistula during connection and disconnection of the patient to the dialyser.
2. Blood samples taken for haematological and biochemical investigations,
together with those taken for various research projects.

(3) Blood loss should a dialyser leak or rupture during use.
(4) The residual blood volume in the dialyser and the blood lines after each dialysis.
(5) Coincidental blood loss (eg gastro-intestinal and menorrhagia) under the influence of anticoagulants.

**Shunt and fistula connection.** The use of both the arteriovenous shunt and the fistula may be associated with the loss of considerable volumes of blood. Lindsay and Burton (1972) found that the amount of blood routinely lost by cannulation of arteriovenous fistulae and by spillage from shunts amounted to 8 ml per dialysis in the hands of experienced operators. Losses in excess of this may occur from time to time with complications such as accidental shunt or connection separation (Kisken et al, 1968) and the occasional episode of severe bleeding after cannulation (Patel et al, 1968; Eisinger et al, 1969). It is obvious, therefore, that a careful technique must be utilised with each cannulation in order to keep this source of blood loss to an absolute minimum.

**Blood sampling.** Hocken and Marwah (1971) state that "biochemical and haematological investigations are a potent source of iron deficiency in patients with chronic renal failure". They estimated that patients undergoing stabilisation on their regular dialysis programme in hospital had blood samples removed for such investigations amounting to well over 3 l per annum. This figure does not take into account research work that many dialysis units, our own included, may carry out. It can well be argued that there is little need for routine haematological and biochemical estimations once the patient is stabilised on dialysis. In fact our home dialysis patients usually have a blood sample taken only once or twice per year. There also may be a case to be made out for rationalising our research so that not all units are investigating all aspects of regular dialysis.

**Dialyser rupture.** Dialyser leakage or bursting is regrettably still a relatively common occurrence. We feel that the responsibility for this problem rests mainly with the manufacturer who must strive to make his disposable dialyser burst-proof; coil users will probably encounter a burst rate varying between 2 and 7% (Muir et al, 1970; Burton et al, 1972). However, a good pre-dialysis pressure testing method in the dialysis unit should help to minimise leakages occurring during dialysis. It is difficult to estimate the volume of blood that is lost when a dialyser ruptures in use. It could amount to the total volume of the dialyser and be in excess of 200 ml, but is usually less as a saline wash-back will recover some of this blood. To measure with precision the volume of blood lost would involve whole-body monitoring of a patient whose red cells were labelled with either $^{59}$Fe or $^{51}$Cr before
and after such a rupture had occurred. There would be serious ethical problems with such a study as one would have to keep a group of patients labelled continuously and await a chance burst. Assuming that 200 ml of blood were lost every time a coil dialyser burst this would amount to each patient losing 600 ml of blood per annum if he was dialysed twice weekly on a coil with a 3% burst rate.

**Dialyser blood loss.** At the end of each dialysis it is inevitable that some blood remains trapped in the dialyser and its blood lines and is not washed back to the patient. Lawson et al (1968), Will et al (1970) and Hocken and Marwah (1971) have suggested that the blood loss in the dialyser is a major source of iron loss to the dialysis patient. While blood requirements for biochemical and other investigations can easily be minimised blood losses in the dialyser are more difficult to reduce. We, therefore, have looked into the factors responsible for blood remaining trapped in the dialyser and wish to devote the majority of this article to the consideration of this problem.

**THE MEASUREMENT OF DIALYSER BLOOD LOSS**

Several workers have reported blood losses in both coil and Kill artificial kidneys by estimating the haemoglobin concentration or the haematocrit found in large volumes of fluid washed through the dialyser after use (Evans et al, 1967; Patel et al, 1967; Muth & Wells, 1969; Nidus et al, 1969; Hocken & Marwah, 1971; von Hartitzsch & Hoenich, 1972; von Hartitzsch et al, 1972a). The method most often employed is to circulate through the dialyser, after the usual wash-back, a known volume of fluid, usually 0.9 g/100 ml saline, for an arbitrary period of time to ensure even mixing of the residual blood within the fluid. Haemoglobinometry is then undertaken on samples of the recirculated fluid and the patient’s own haemoglobin value is measured. The blood volume in the dialyser may then be calculated as follows:

\[
\text{Dialyser blood volume} = \frac{F}{P} \times \text{volume of recirculate}
\]

where:

- \( F \) = haemoglobin concentration in the recirculating fluid (g/100 ml)
- \( P \) = patient’s haemoglobin concentration (g/100 ml)

The accuracy of such a technique is open to question. The technique obviously assumes that all blood remaining in the dialyser is washed into solution and even should this be the case it cannot be easy to mix completely a few ml of red cells in one litre of wash-out fluid then to obtain representative samples for measurement. Will and his colleagues (1970) discussed this technique and felt that results so obtained were "so inaccurate as to be meaningless". Nevertheless it is still not uncommon to see blood loss figures derived in this way quoted to two decimal places; for example von Hartitzsch et al (1972b) quote the mean blood loss in the Meltec multipoint
Figure 1. Measurement of dialyser blood loss: comparison of measured and actual blood volumes using the haemoglobinometry technique. (Reproduced from Lindsay et al (1972a) with permission of the Editor, Clinical Nephrology)

Figure 2. Measurement of dialyser blood loss: accuracy of haemoglobinometry and radio-chromium red blood cell techniques. (Reproduced from Lindsay et al (1972a) with permission of the Editor, Clinical Nephrology)
dialyser to be 0.85 ml. We have used this technique to estimate known blood volumes in 1 litre of 0.9 g/100 ml saline (Lindsay et al., 1972a). The results of this experiment are plotted in Figure 1 and it can be seen that the accuracy of the technique is in the order of ± 100-500% when attempting to measure blood volumes less than 5 ml and even when volumes of 25 ml are measured the accuracy is no better than ± 30% (Figure 2).

Two groups of workers (Will et al., 1970; Muir et al., 1970) have separately used techniques involving radioactive labelled red cells for the estimation of dialyser blood loss. Will and his colleagues (1970) used both $^{59}$Fe and $^{51}$Cr labelled red cells and a whole body monitor whereas Muir et al (1970) used $^{51}$Cr labelled red cells and a large well scintillation counter into which they placed cans containing the dismantled dialysers. We have assessed the accuracy of both techniques and found them to be highly accurate and in good agreement with each other (Lindsay et al., 1972a) (Figure 3). The accuracy of these techniques is such that losses of over 3 ml can be estimated with an error not more than ± 16% (Figure 2). Red cell labelling with $^{51}$Cr is a simple process taking little time and has an advantage over $^{59}$Fe in that it can, in vivo, be carried out on the day of dialysis whereas some two weeks must be allowed for the incorporation of $^{59}$Fe into the red cells. The only disadvantage from the use of such isotopic techniques is the necessity for good counting equipment and also that radioisotopes have to be given to

![Figure 3. Measurement of dialyser blood loss: comparison of measured and actual blood volumes using two radio-chromium red blood cell techniques; (method 1 – Will et al., 1970; method 2 – Muir et al., 1970). (Reproduced from Lindsay et al (1972a) with permission of the Editor, Clinical Nephrology)
patients. We would submit, therefore, that these techniques should not be used routinely in all units but should be limited to units engaged in comparative evaluation studies.

**Blood loss characteristics of various dialysers.** Using the radio-chromium technique described by Muir et al (1970) we have measured the blood loss in several commonly used dialysers (Lindsay et al, 1972b). The results of this study are summarised in Table I. Examination of this table shows that in the majority of dialysers the blood loss per dialysis is under 10 ml. It must be appreciated, however, that such a figure still represents an annual loss in excess of 1 litre. It would also appear that coil dialysers on the whole tend to be associated with slightly lower blood losses than parallel flow dialysers. Two commercially available disposable dialysers are seen to have what we would term excessively high blood losses. These are the original

<table>
<thead>
<tr>
<th>Dialyser</th>
<th>Membrane</th>
<th>Blood loss (ml) mean ± SD</th>
<th>Number studied</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parallel flow</td>
<td>Cuprophane</td>
<td>11 ± 7</td>
<td>18</td>
</tr>
<tr>
<td>Watson Marlow Kill</td>
<td>PT 150</td>
<td>6 ± 2</td>
<td>6</td>
</tr>
<tr>
<td>Cobe Mini Kill</td>
<td>PT 150</td>
<td>6 ± 3</td>
<td>10</td>
</tr>
<tr>
<td>Bühse Poulenc</td>
<td>PT 150</td>
<td>30 ± 4</td>
<td>18</td>
</tr>
<tr>
<td>Gambro Alwall</td>
<td>PT 250</td>
<td>16 ± 6</td>
<td>10</td>
</tr>
<tr>
<td>Gambro Alwall*</td>
<td>PT 250</td>
<td>4 ± 1</td>
<td>6</td>
</tr>
<tr>
<td>Gambro Lundia</td>
<td>PT 250</td>
<td>4 ± 1</td>
<td>6</td>
</tr>
<tr>
<td>Coils</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Travenol Ultra Flo 100</td>
<td>PT 150</td>
<td>7 ± 1</td>
<td>5</td>
</tr>
<tr>
<td>Travenol Ultra Flo 100</td>
<td>PT 300</td>
<td>7 ± 1</td>
<td>10</td>
</tr>
<tr>
<td>Travenol Ultra Flo 145</td>
<td>PT 300</td>
<td>5 ± 2</td>
<td>6</td>
</tr>
<tr>
<td>Nephron R70</td>
<td>PT 150</td>
<td>7 ± 2</td>
<td>5</td>
</tr>
<tr>
<td>Extracorporal EX-03</td>
<td>PT 150</td>
<td>4 ± 2</td>
<td>9</td>
</tr>
<tr>
<td>Hollow fibre</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cordis Dow</td>
<td></td>
<td>20 ± 10</td>
<td>7</td>
</tr>
</tbody>
</table>

* Results obtained from dialysers using efficient heparinisation and washback techniques

* Not commercially available with PT 250 membranes

Gambro-Alwall dialyser (Ab Gambro, Lund, Sweden), now obsolescent, and the Cordis Dow hollow fibre kidney. The regular use of either of these dialysers will result in annual blood losses of over 2 to 3 litres. In addition to this value one must consider a further volume of blood remaining trapped within the blood lines. We have measured this for the majority of the lines associated with the various dialysers and found the loss to average 3 ml per dialysis (Lindsay et al, unpublished results).

**FACTORS RESPONSIBLE FOR BLOOD TRAPPING WITHIN DIALYSERS**

There are two main factors responsible for dialyser blood loss. Firstly,
manifold designs may induce mechanical hold-up of anticoagulated blood. Each dialyser design will have its own particular problems which, to some degree, may be overcome by using different wash-back techniques and it is obviously essential to ascertain the optimum technique for each dialyser. Cole et al (1962) and Evans et al (1967) separately found that they were able to reduce the blood loss in the standard Kill simply by running the dialyser in a vertical position for the last half hour of dialysis keeping it so during the wash-back procedure. It is of significance that Cole and his colleagues (1962) found this reduction in dialyser blood loss to be associated with the halving of their patients' transfusion requirements. Will et al (1970) found that blood loss could be reduced in the Ultra-Flo 100 (Travenol) coil by removing the coil from its container and placing it on its side during the wash-back procedure. They also noted that a further reduction in blood loss could be obtained by using 5 g/100 ml dextrose as wash-back fluid in place of 0.9 g/100 ml saline. They were unable, however, to offer any explanation for this latter finding. Chavamian and his colleagues (1972) also found that the blood loss in coil dialysers could be reduced by running the coil in the horizontal position while Nidus et al (1969) reduced their coil blood losses by using a combined saline wash and air blow-out technique. There is no doubt that different operational and wash-back procedures will influence the volume of blood left in the dialyser. For example, the two groups (Will et al, 1970; Muir et al, 1970) who separately developed the radio-chromium techniques for the estimation of dialyser blood losses surprisingly quoted widely different figures for the blood loss caused by the Ultra-Flo 100 (Travenol) coil. Will et al (1970) estimated the mean whole blood loss to be 30 ml per dialysis while Muir et al (1970) found a value of only 6.6 ml. Our studies (Lindsay et al, 1972a) have demonstrated that both methods of blood loss measurement were in agreement and highly accurate (Figures 2 and 3). We conclude, therefore, that the difference in the blood losses reported by these groups was not a factor of errors in methodology but rather related to differences in dialysis running and wash-back techniques.

The second factor responsible for dialyser blood loss is the development of thrombus on the dialysis membranes. If the Gambro-Alwall dialyser is dismantled after use variable amounts of thrombus are found partially adherent to the dialysis membranes; this is especially marked at the venous or outlet end of the dialyser (Figure 4). The use of a scanning electron microscope demonstrates fibrin-like strands trapping red blood cells (Figure 5). Further studies (Lindsay et al, 1972, unpublished results) using fluorescein labelled antifibrinogen serum have confirmed that these strands are fibrin. It is interesting that fibrin formation can take place in spite of adequate heparinisation; during these experiments the patients' whole blood clotting times measured by the Lee and White technique, was always in excess of
thirty minutes. This thrombus formation is also associated with changes in the haemostatic status of the patient over the course of a dialysis (Lindsay et al, 1972, unpublished results). A considerable fall in the platelet count is seen, with an elevation of factor V and a fall in the plasminogen level. The rise in factor V is associated with a fall in the partial thromboplastin time and indicates activation of the coagulation cascade mechanism, while the fall in plasminogen suggests that the fibrinolytic system has been activated by the presence of fibrin. It is interesting that post-dialysis falls in platelet count and plasminogen levels in the patient may be indications of thrombus
Table II. Factors influencing intra-dialyser thrombus formation and blood loss

<table>
<thead>
<tr>
<th>Dialyser and Membrane</th>
<th>Fall in platelet count</th>
<th>Fall in plasminogen level</th>
<th>Blood linear velocity</th>
<th>Thrombus formation</th>
<th>Bloos loss</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gambro-Alwall PT 325</td>
<td>+++</td>
<td>+</td>
<td>Low</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Gambro-Lundia PT 250</td>
<td>+</td>
<td>-</td>
<td>Low</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Cordis Dow</td>
<td>+++</td>
<td>-</td>
<td>Low</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Rhône-Poulenc PT 150</td>
<td>+</td>
<td>-</td>
<td>Low</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Ultra Flo 100 PT 300</td>
<td>++</td>
<td>-</td>
<td>High</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>EX-03 PT 150</td>
<td>-</td>
<td>-</td>
<td>High</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

formation on the membranes which, in turn, is invariably associated with a high dialyser blood loss (Lindsay et al., 1972, unpublished results) (Table II). If much thrombus formation has taken place upon the dialysis membranes then the volume of blood remaining in the dialyser is unlikely to be influenced to any extent by either the technique or the volume of the wash-back. We have demonstrated this by using increasing volumes of saline in an attempt to reduce the blood loss caused by the Cordis Dow hollow fibre dialyser (Figure 6).

![Figure 6. Relationship between wash-back volume and the residual blood volume of the Cordis Dow hollow fibre kidney. Results: mean values of four experiments. (Reproduced from Lindsay et al (1972b) with permission of the Editor, Clinical Nephrology)](image-url)
THE CAUSES OF THROMBUS FORMATION ON DIALYSIS MEMBRANES

It has been known for years that blood circulating within the body has, effectively, an infinite clotting time. However, when blood comes in contact with a foreign surface, coagulation may occur within minutes. In recent years there has been a search for artificial surfaces of low thrombogenicity for use in cardiovascular surgery but there has been comparatively little interest in the thrombogenicity of the materials used in the extracorporeal circuit of the artificial kidney.

Role of platelets. We have found both in vitro, using a membrane test cell system, and in vivo, using $^{51}$Cr labelled platelets, that platelets readily adhere to cellulose-based dialysis membranes (Lindsay et al, 1972, unpublished results). Furthermore, we have demonstrated that the reduction of platelet adhesiveness following the oral administration of antiplatelet agents (soluble aspirin and dipyridamole compounds) is associated with retention of fewer platelets on the dialysis membranes and, thus, the patient's platelet count falls less over the course of a Gambro-Alwall dialysis. There is also less thrombus formed on the membranes with a consequent reduction in the dialyser blood loss (Lindsay et al, 1972, unpublished results). These observations suggest that platelet retention by the dialysis membrane is an important early step in a reaction which may proceed to thrombus formation even in the presence of heparin.

Linear velocity of blood. The linear velocity of blood travelling across the membrane surface may also influence thrombus formation upon that surface. Muir (personal communication) carried out experiments using the Ross–Muir dialyser and found that thrombus formation occurred on cellulose-based membranes if the average linear blood velocity fell below 5 cm/sec and remained so for periods of five hours. These experiments were carried out in vivo with fully heparinised circulating blood. He and his colleagues (1970) suggested that a low blood linear velocity was the major factor in the high blood loss of the Gambro-Alwall dialyser. We now doubt that this is the case for the linear velocity of blood passing through other parallel-flow dialysers, eg Rhône-Poulenc, Kiil, Gambro-Lundia and Cobe mini-Kiil, is under 5 cm/sec and these dialysers do not have a problem with in vivo thrombus formation. However, the linear blood velocity may be of secondary importance in a situation where the dialysis membranes cause much retention of platelets, a slow velocity encouraging thrombus formation while a high velocity is protective. For example, the Ultra-Flo 100 (Travenol) coil with PT 300 membranes causes a significant fall in the platelet count yet, unlike the Gambro-Alwall situation, relatively little thrombus formation takes place (Table II). On the other hand, the EX-03 coil, with PT 150 membranes, has, in clinical
use, the same blood linear velocity but does not cause a significant fall in platelet count after dialysis. These factors suggest that the nature of the surface itself is of major importance and this will be discussed next.

Nature of dialysis membrane. Many workers, including Lyman et al (1968, 1969) and Rodman and Mason (1970a, 1970b) have carried out extensive studies on thrombus formation upon materials used in cardiovascular surgery (eg PTFE, silicone rubber) as part of the Artificial Heart Programme (Institutes of Health, Bethesda). These workers suggest that platelet retention to these materials is an important step in thrombus formation and Salzman (1971) states "it is now customary to view surface-induced thrombosis as chiefly, if not exclusively, a platelet problem". Less attention has so far been given to the thrombogenicity of materials used in haemodialysers although Mason et al (1972) have carried out ex vivo experiments which support our work by demonstrating that haemostatic changes occur when blood comes in contact with Cuprophane membranes. Because the reaction between the platelet and the dialysing membrane appear to be of importance in thrombus formation we have attempted to quantitate this reaction in vitro. A membrane test cell system has been constructed (Figure 7) and we have standardised a method whereby citrated blood may be introduced between two layers of dialysis membrane; the test cell is then sealed and rocked from side to side in a standard fashion for a standard time. After withdrawing the blood from the test cell the pre- and post-contact platelet counts may be compared; a fall in the platelet count indicating the number of platelets retained by the membranes. On expressing the fall in platelet count as a per-

![Figure 7. Diagram of membrane test cell. (Reproduced from Lindsay et al (1972c) with permission of the Editor, British Journal of Haematology)](image-url)
percentage of the initial platelet count a value for platelet adhesiveness is obtained. We have found that this method has advantages over a standard glass bead column method (Hirsh et al., 1966) as a test for platelet adhesiveness (Lindsay et al., 1972c). Using twin test cells of identical construction and a rocking device (Figure 8) paired estimations for platelet adhesiveness can be made on divided blood samples. If both test cells contain standard membranes (Cuprophan PT 300, J P Bemberg) an excellent correlation is obtained between the two sets of results indicating that the method has little intrinsic error (Figure 9). A test membrane may then be inserted into one test cell and compared directly with the standard PT 300 membrane by examination of paired results for platelet adhesiveness. In Figure 10 Cuprophan PT 250

CALIBRATION OF TEST CELL METHOD — USING PT 300 MEMBRANE

<table>
<thead>
<tr>
<th>% PLATELET ADHESIVENESS BY TEST CELL 'A'</th>
<th>% PLATELET ADHESIVENESS BY TEST CELL 'B'</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>20</td>
<td>20</td>
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<tr>
<td>30</td>
<td>30</td>
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<tr>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>50</td>
<td>50</td>
</tr>
</tbody>
</table>

$y = 1.07x - 1.83$

$r = 0.88$

Figure 9. Calibration of test cell method: paired results for platelet adhesiveness using Cuprophan PT 300 membranes. (Reproduced from Lindsay et al (1972c) with permission of the Editor, British Journal of Haematology)
(J P Bemberg) is compared with PT 300; the results indicate a linear relationship between the two sets of results and a paired 't' test demonstrates that fewer platelets adhere to the PT 250 membranes. In a similar experiment we have found that Cuprophan PT 325 has a greater platelet attraction than PT 300 (Lindsay et al, 1972, unpublished results). This suggested that Cuprophan PT 250 membranes might be less thrombogenic than the PT 325 membranes used in the standard Gambro-Alwall dialyser. With the cooperation of Ab Gambro (Lund, Sweden), Gambro-Alwall dialysers containing PT 250 membranes were prepared and these were found to have less thrombus formation and a lower blood loss (Table I; Lindsay et al, 1972, unpublished results). Studies such as these suggest that the membrane test cell is of potential value in the evaluation of the potential thrombogenicity of different dialysis membranes. At present we are unable to state why there is a variable retention of platelets by different membranes but the surface charge (Sawyer & Pate, 1953; Srinivasan & Sawyer, 1970) or the surface free energy (Lyman et al, 1968) may be among important determinants.

Configuration of membrane surfaces. In our experience a variable percentage of the hollow fibres of the Cordis Dow artificial kidney, which is of novel design, may contain a considerable quantity of thrombus (Figure 11) and we (Tables I and II) and others (Möhring et al, 1972; Bosch et al, 1972; von
Hartitzsch et al, 1972a) have found, in consequence, a rather variable but undesirably high blood loss with its use. There may be intrinsic thrombo- genic problems with the nature of the materials used in the manufacture of the capillary tubes and there may also be difficulty in obtaining absolutely uniform tube diameter throughout the length of every individual fibre.

**Form of anticoagulation.** The use of anticoagulants other than heparin as a means of reducing thrombus formation merits consideration. Long-term oral anticoagulants, such as Warfarin, given in addition to heparinisation during dialysis may reduce thrombus formation by their action on the vitamin K dependent factors but there is dispute as to whether they have any significant antiplatelet effect (Hellem & Stormorken, 1969) which may be of greater importance. Furthermore the serious complications of long-term anticoagulation are well known in dialysis units from the days when arteriovenous shunts were commonly used. Arvin, with its unique effect upon fibrinogen, has been used in place of heparin as an anticoagulant during dialysis and was observed to reduce the formation of fibrin on, and the retention of white blood cells by, the membranes of a Kiil dialyser (Hall et al, 1970). However, it would be impractical to use this drug routinely for dialysis as its administration is more complex than heparinisation and, as it is not easily neutralised, the patient would have a hypofibrinogenanaemic clotting defect for some time after dialysis which might, inter alia, lead to a high blood loss from arteriovenous fistula cannulation sites. The use of antiplatelet preparations, such as soluble aspirin on a long-term basis, can reduce dialyser blood loss.
(Lindsay et al, 1972, unpublished results) but the risk of side effects such as gastrointestinal bleeding is a contra-indication. We do not think, therefore, that any changes in the current policy of anticoagulation during dialysis are indicated for, in the majority of cases, dialyser thrombus formation is minimal and, therefore, the use of heparin is satisfactory. It is more logical to identify and use less thrombogenic materials within dialysers than to attempt to reduce thrombus formation by drugs.

CONCLUSIONS

It has been the aim of this editorial to stress the importance of blood loss to the regular dialysis patient. The magnitude of this blood loss is often not appreciated. Assuming twice weekly dialysis and approximate blood losses of 3 ml trapped in blood lines + 5 ml blood sampling + 8 ml loss from the arteriovenous fistula, then using dialysers with 'intrinsic' blood losses of 5 ml and 30 ml respectively will lead to annual blood losses in excess of 2 litres in the former case and 4.5 litres in the latter case. It is little wonder that our dialysis patients remain so anaemic. We would suggest that both the clinician and the manufacturer must give greater consideration to blood loss in these patients. The clinician should minimise his investigations; take scrupulous care with the use of arteriovenous shunts and fistulae; carry out thorough pre-dialysis pressure testing to eliminate ruptures during dialysis; and develop the optimum wash-back technique for the dialyser that he is using. The manufacturer should consider the materials used in his dialyser with regard to their thrombogenicity; the manifolding of the dialyser which should be such as to allow an efficient wash-back with the minimum volume of fluid; and, in the case of disposable dialysers, should have an efficient pressure testing procedure.

Finally, we would suggest that any clinical unit doing basic evaluation work on dialysers should, in addition to determining clearance and ultrafiltration characteristics, measure the blood loss accurately and, if found to be high, try to establish the reasons.

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